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VOL. I.—30TH YEAR. SYDNEY, SATURDAY, MARCH 27, 1943. No. 13.[1] See footnote, page 267.

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VOL. I.—30TH YEAR. SYDNEY, SATURDAY, MARCH 27, 1943. No. 13.[1]

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THE INVESTIGATION OF RENAL FUNCTION WITH A NEW NOMOGRAPHIC METHOD FOR THE DETERMINATION OF UREA CLEARANCE.[1]

By MORRIS C. DAVIS, M.D., M.R.A.C.P.,
Honorary Out-Patient Physician, Alfred Hospital, Melbourne.

> Sometimes without any treatment, the more obvious and distressing of these symptoms disappear . . . are gradually lost sight of or are absolutely forgotten.—R. BRIGHT, "Medical and Surgical Monographs", 1838.

THE inspiration for this paper came from the perusal of results obtained over the past few years by the use of a modification of the Van Slyke method of the urea clearance test. The possibility of correlating biochemical, microscopic and clinical findings in every case of the series allowed for a useful survey of the relative value of all tests on the assessment of renal function.

Except for certain of the clinical histories, all the data relating to the cases mentioned have been obtained from tests made by myself.

THE MEANING OF THE TERM "CLEARANCE".

The term "clearance" in general represents that volume of blood which holds the amount of material excreted in a given time. If we assume that the kidney is capable of removing all of a substance from the blood which is delivered to it, then the term "clearance" would represent that volume of blood which can be so dealt with by the kidney in unit time.

Thus urea clearance represents the amount of blood which the kidney in given time is capable of completely clearing of urea. A similar definition can likewise be used for creatinine clearance, xylose clearance and others. Substances for which the kidney has a selective reabsorption (such as the threshold substance glucose) cannot be used for clearance tests, because no glucose will be excreted until a certain blood level is reached. If glucose is to be used, it has first to be converted into a non-threshold substance by phloridzin, which prevents selective reabsorption of glucose by the kidney tubules.

The mode of determining clearance is helpful to the understanding of the term. If, under conditions of uniform activity, the quantity of urea which a completely functioning kidney excretes in a given time is estimated, and if the blood urea content at the time of such excretion is known, then it is possible to estimate the volume of blood which contains this quantity of urea. If it is presumed that all the urea delivered to the kidney is eliminated, then this volume would be the smallest possible volume of blood that would have to be delivered to and dealt with by the kidney, and this quantity is called the clearance. Clearance should therefore be defined as the estimated minimum volume of blood which the kidney is capable of clearing of urea in unit time.

Addis and Shevky in 1922[(1)] showed that the blood in the renal vein has only slightly less urea than that in the jugular vein, and therefore they proved that the kidney is incapable of completely eliminating all the urea delivered to it. This nullifies the significance of the clearance volume as an absolute quantity, but is quite immaterial to our accepting it as a relative standard. As an example, we shall find later that the clearance (or estimated minimum volume of blood dealt with by the kidney) under certain conditions is 75 cubic centimetres. If the kidney in actual fact can deal with only one-tenth of the urea delivered to it, then the volume of blood to be cleared of urea would be 750 cubic centimetres. The multiplying factor of ten, however, would have to be used in every case including the normal, and so in the calculation of the final result as a percentage of normal it would be nullified. The estimated minimal volume may therefore be regarded as an arbitrary standard, the normal being fixed and the clearance for any other case being taken as a percentage of this. It is strictly correct to speak of clearance only in terms of such percentage and not in terms of volume.

[1] Abridged from a paper which made the subject of the Bertram Armytage Prize for Medical Research at the University of Melbourne, 1942.

[1] The issues of March 6, 13 and 20, 1943, were incorrectly numbered; they should have been respectively Numbers 10, 11 and 12.—EDITOR.

Historical Review.

For a proper understanding of the test it will be necessary to trace the development of the conception of urea clearance.

Ambard[1] in 1910 attempted to establish precise laws governing the excretion of urea from the kidney. It was maintained that, if the concentration of a substance in the blood and urine was known, the action of the normal kidney could be anticipated with mathematical accuracy. The kidney was said to possess no intrinsic variability of function. Thus in 1912, Ambard and Weil,[2] in a complicated and unwieldy formula, produced their coefficient of renal function. Because it did not account for many of the variable factors this formula proved unsuccessful, but by focusing attention on the necessity to collate the level of a substance in the blood with its rate of excretion in the urine, it set an exceedingly valuable principle for the determination of renal function.

Four years later Addis and Watanabe,[4] studying the rate of excretion of urea by healthy adults receiving a constant diet (75·1 grammes of protein, 120 grammes of fat, 220 grammes of carbohydrate and 1,710 cubic centimetres of water), found that the average amount excreted became uniform after twenty-four hours—that is, that the patient established a nitrogenous equilibrium. After urea has been given by mouth, this average amount excreted rises. A certain degree of variability that existed in the comparison between different subjects was explained as being due to different levels of protein catabolism in individual cases. The same degree of variability occurred before and after the administration of urea, and it was found that so long as water was available and conditions were constant, the rate of the excretion of administered urea would increase in proportion to the amount of urea ingested. Thus, while within the limits of dosage available it is impossible to reach the absolute capacity of the normal kidney to excrete urea, each kidney under constant conditions will act in the same way.

In the following year Addis and Watanabe[5] applied these findings to the problem of renal function. They introduced the ratio

$$\frac{\text{grammes of urea in one hour's urine}}{\text{grammes of urea in 100 cubic centimetres of blood}}$$

as an indication of renal function, and they emphasized the following three very important conditions which were necessary for its accuracy: (i) The ratio varies with such controllable factors as the intake of food and water, and these must therefore be standardized. (ii) In dealing with urea excretion, other variables should be reduced, or the urea factor should be so increased that other variables become relatively negligible. (iii) The test should be carried out under conditions which accentuate the difference in renal function between two given subjects.

The first condition is attained by performing the test on the fasting patient, and the remaining conditions are attained by increasing the measurable factor (urea) and so relatively reducing the others. In connexion with the third requirement, Addis and Watanabe state that "the effect of lesser degrees of anatomical defect may only be revealed by subjecting kidneys to the strain of a maximal call on their functional capacity". In proof of this fact an experiment is described in which one ureter of a rabbit is ligated. The ratio calculated before and after ligation showed that if one kidney was inactivated, the reduction in total renal function was made evident only by the administration of urea, since under such conditions the one active kidney could not cope with the added strain of excreting this urea, and a decrease in the ratio $\frac{\text{amount excreted}}{\text{amount in blood}}$ resulted. Addis and Watanabe in this connexion make the following statement:

> This experiment illustrates an important principle in measuring renal function—that function may be normal under ordinary conditions, yet defective under strain. The administration of a large quantity of urea before the test therefore, has not only the advantage of tending to equalise experimental conditions, it may also serve to bring latent deficiency to light.

It is of the utmost importance to emphasize this aspect of the test.

In 1922 Addis[6] made the further comment that the "fundamental" principle applicable to all function methods had been entirely neglected—the maximal effort of which the organ to be tested was capable. The ratio was applied to human subjects after the administration of 1,000 cubic centimetres of water and of amounts of urea varying from 30 grammes to nil, according to the amount of urea in the fasting blood. Specimens of blood and urine were taken at the fourth, fifth and sixth hour after the administration of urea, and it was found that the amount of urea excreted in one hour's urine was directly proportional to the amount of urea in 100 cubic centimetres of blood, and that the ratio $\frac{\text{urea in one hour's urine}}{\text{urea in 100 cubic centimetres of blood}}$ indicated closely the amount of functioning tissue in the kidney, provided always that the urea-excreting capacity of the kidney was subjected to strain. Taylor, Drury and Addis,[7] in 1923, confirmed this fact, and found that the normal ratio varied from 40 to 55; this means that under "Addis" conditions the human kidney will excrete as much urea in one hour as is contained in 40 to 55 times 100 cubic centimetres of blood.

In the years 1918-1919, Maclean and De Wesselow,[8] in the paper in which nephritis was divided into its two celebrated types, hydræmic and azotæmic, recorded certain biochemical observations in cases of war nephritis. They introduced the well-known urea concentration test, and laid special emphasis on the percentage of urea in the urine after 15 grammes of urea had been given by mouth. The problem of low concentrations of urea due to diuresis was overcome by emphasizing the fact that it might be necessary to wait up to three hours until diuresis was over. If diuresis persisted beyond that point then a defective kidney function was probable. It is well to note the entire reliance and emphasis placed on the sole figure of urea concentration. In 1920[9] Maclean and De Wesselow severely criticized the Ambard coefficient as follows:

> When the blood urea concentration is higher than normal, the urea coefficient rises with it, but it is only a waste of time and labor to utilise a complicated mathematical formula when the same information can be obtained from the blood urea.

Thus it appears that Maclean and De Wesselow in 1920 were unaware of the much simpler formula which Addis had suggested four years earlier.

The present conception of urea clearance began in 1921 with the work of Austin, Stillman and Van Slyke.[10] In an essentially mathematical discussion it was shown that the direct ratio between the blood urea content and urea excretion rate held only with volumes of urine exceeding two cubic centimetres per minute. When the amount of urine was below this volume (termed the augmentation limit), the urea excretion rate fell in proportion to the square root of the volume.

Moller, McIntosh and Van Slyke in 1928[11] and 1930,[12] with their preceding work as a basis, described their urea clearance test, known generally as the Van Slyke urea clearance test. They attempted to simplify the procedure of Addis, they introduced a modification for volumes of urine under two cubic centimetres per minute (the term standard clearance being applied to the latter and maximum clearance to the higher volumes), and they regarded the necessity for diuresis as described by Addis as non-existent. By the introduction of the maximum and standard figures, it was possible to determine kidney function in terms of a percentage of average normal function. The test allowed for a wide degree of variability in normal and abnormal results, as follows:

> 70% to 100% was regarded as normal.
>
> 50% to 70% was regarded as mild renal failure.
>
> 20% to 50% was regarded as moderate renal failure.
>
> 0% to 20% was regarded as severe renal failure.

This test has been given considerable trial in England and America, and results have been variable. Urquhart and McCollum,[13] in 1935, stated that "figures under 20%

indicated a bad prognosis, but moderate lowering did not help any more than repeated simple blood urea estimations".

By this time also a certain degree of irregularity of results was noticeable. Thus Don[14] concluded that "failure of the tests to agree closely with one another suggests either that they are not completely reliable or that different renal functions are being measured". Written in 1937, these conclusions were based on the original Van Slyke clearance test. Under conditions of this test, the kidney was not subjected to strain, and no approach to Addis conditions was attempted.

Three years earlier, however, Fowweather,[15] without reference to the work of Addis, found that, whereas in 50 normal subjects the Van Slyke test produced figures varying from 29% to 101%, when the test was carried out after urea had been given by mouth (second-hour estimations of the blood urea level and urea concentrations being used), the variations in the results obtained from the same subjects was between 73% and 120%. When the Van Slyke test gave results below normal, the modified test gave a truer indication of the functional capacity of the kidney. Thus, when the kidney was subjected to strain, a considerable narrowing of the range of values was obtained among healthy subjects. If Fowweather had his subjects at complete rest during these tests, an even smaller variation in the range of normal figures would have been obtained, for it has been shown that with change of posture considerable variability in renal activity occurs. Fowweather[16] summarized the position with these words:

> I am convinced that the urea clearance test is a much better index of renal function than the tests formerly in use—I believe it to be in fact the best renal function test that we possess.

Cope,[17] in a paper which gave due value to the work of Addis, concluded in identical strain:

> It is admitted that the renal function test most helpful to the individual clinician is as a rule the one in whose interpretation he has had most experience; the urea clearance test, however, appears to be the most rational assessment of renal function that we at present possess.

The remarkable agreement which has been found to exist between the results of the urea clearance test after urea has been given by mouth, of the creatinine clearance test and of the xylose clearance test—an agreement not found under simple Van Slyke conditions—supports the view that the modified urea clearance test is sound, reliable and accurate, and that there is ample justification for dispensing entirely with the calculation of clearance values without the administration of urea.

A brief account of other useful or satisfactory tests of renal function should be given at this stage. Of these, Joly,[18] in 1932, places reliance on the quantity of urea eliminated during each of the second and third hours after a draught of urea. "No matter how high the concentration may be, the response to the test must be considered bad unless more than 1/10 of the original dose of urea is eliminated each hour". A patient with low urea concentration, but eliminating a large quantity, is safer than one in whose case the reverse holds. "I have not had a death from uræmia following prostatectomy in any case where the elimination of the urea was more than 1·5 grams each hour even though the urea concentration was under 2%."

Joly's figures, of course, show that in the assessment of the value of urea concentration, volumes of urine must be taken into consideration. However, no test estimating the power of the kidney to excrete urea can be really accurate if it disregards the height of the blood urea level during the period tested. Joly is able to separate subjects fit for operation from those unfit, and undoubtedly his figures are a valuable guide; but it can be shown that a certain number of subjects proved unfit by this method might have been proved fit by a more accurate assessment of renal reserve power.

The total amount of urea excreted in three hours after urea has been given by mouth has been utilized by Krieger[20] for the estimation of renal function in pregnancy. A careful analysis leads to the conclusion that this test improves on the use of the urea concentration test alone; however, it does not take into consideration the height of the blood urea level and it gives no assessment of "renal reserve".

Krieger[21] agrees that the Fowweather test is a useful guide to renal function and that considerable agreement exists between the total amount of urea excreted in three hours and the results of the Fowweather test. The total amount of urea excreted in three hours may therefore be a useful adjunct to the Fowweather test. The extra hour required for collection of urine and the neglect of the blood urea content during the test are disadvantages which do not outweigh any advantages it may possess.

Determination of Clearance.

If U represents the amount of urea in a unit volume of urine (cubic centimetre) and V the volume (in cubic centimetres) of urine excreted per minute, then UV represents the amount of urea excreted per minute. If B represents the amount of urea in a unit volume (cubic centimetre) of blood, then $\frac{UV}{B}$ represents the minimum number of unit volumes of blood which would have to be dealt with by the kidney. This figure, which was defined as the estimated minimum volume of blood cleared of its urea per minute, is called the urea clearance. Van Slyke has found that the rate of clearance varies with the volume output of urine. When this volume is over two cubic centimetres per minute (called the augmentation limit), the average normal clearance is 75 cubic centimetres, while when the volume is under two cubic centimetres per minute the average normal clearance is 54 cubic centimetres. In the latter case, it has been shown that the rate of excretion is proportional to the square root of the volume of urine passed; hence the formula for these figures is $\frac{U\sqrt{V}}{B}$. The clearance obtained with larger volumes is called the maximum clearance, the former the standard clearance. For purposes of comparison, the figures 75 to 54 cubic centimetres being taken as average normal values, the results are estimated as a percentage of average normal function. For example:

U (urea concentration) = 1·0 gramme per 100 cubic centimetres.

V (volume of urine) = 3·0 cubic centimetres per minute.

Then UV = 30 milligrammes of urea excreted per minute.

If B (the blood urea content) is 40 milligrammes per 100 cubic centimetres (0·4 milligramme per cubic centimetre), then the estimated minimum number of cubic centimetres of blood that must pass through the kidney would be $\frac{30}{0{\cdot}4}$ = 7·5 cubic centimetres. The clearance thus expressed as a percentage is 100%.

Some criticism has been levelled at the use of the square root formula, since it has been stated that values in the region of two cubic centimetres per minute (for example, 1·9 and 2·1 cubic centimetres) would cause considerable difference in the results. However, if the formula $\frac{UV}{B}$ is used with the result as a percentage of 75 cubic centimetres (maximum clearance) and $\frac{U\sqrt{V}}{B}$ is used with the results as a percentage of 54 cubic centimetres, identical results are obtained. In other words, if the renal function is expressed as a percentage of average normal value, the use of the square root formula introduces no discrepancy into the result. (See also comment on nomographic chart.)

It is necessary to amplify a further important point. In the simplification introduced by Van Slyke, the subjection of the kidney to a load (Addis conditions) was not regarded as essential. We have seen the theoretical objections to this view, and also the narrowing of the range of the "normal" figures obtained after urea had been given

(Fowweather). A simple analogy may illustrate the necessity of obtaining a maximal functioning organ. In two muscles, one able to raise a maximum of 50 pounds and another 75 pounds, no difference will be revealed until they are subjected to a trial load of 51 pounds, when the difference in strength will at once be revealed. Physiological confirmation of the same principle has been observed in the kidney itself, for Richards[32] and Schmidt[33] established direct proof that in the frog's kidney a varying number of glomeruli function at any given time. Under the influence of urea an increased number come into action.

Suppose when larger and larger quantities of urea are given by mouth a point is reached at which the maximum function will have been exceeded, then an abnormal kidney will reveal itself by the following criteria: (*a*) a pronounced rise in the blood urea level two hours after the ingestion of urea; (*b*) a small volume of blood cleared of its urea—that is, a poor response to the clearance test.

Thus a kidney which can excrete the nitrogenous waste under ideal conditions (subject at rest, bland diet *et cetera*) may be unable to cope with the stress of a severe genito-urinary operation such as prostatectomy. The simple Van Slyke test may not identify this variety of case, whereas the modified test, by subjecting the kidney to conditions of strain, will do so. To quote Addis[4] once again: "The administration of a large quantity of urea before the tests, therefore, has not only the advantage of tending to equalise experimental conditions, it may also bring latent deficiencies to light."

Points of Importance in the Routine Method.

It can be seen that it is very important to obtain exact volumes of urine. The bladder must be completely emptied just prior to the giving of urea, and the urine must be collected exactly one hour, two hours and if necessary three hours afterwards. As a precaution, the times of collection should be recorded on each specimen jar; in this way the problem of exact hour periods may be overcome and some elasticity in collecting times introduced. The patient should be instructed to hold the urine for at least four hours prior to the commencement of the test, preferably overnight. This allows a sufficient flow of urine to ensure emptying of the bladder before the urea is given. In all cases an early morning specimen should be collected for specific gravity measurements and microscopic examination.

If the patient is in bed, he must be made to sit up to pass the hourly specimens. In cases of enlarged prostate, one should not hesitate to catheterize the patient's bladder to obtain the total volumes of urine; indeed, catheterization is necessary in any case in which the completeness of emptying is in doubt. The whole volume for each hour must be kept, and not merely a small representative amount. In the transferring of the urine from receptacle to bottle for transmission to the laboratory, great care should be taken to avoid loss by spilling.

All these points of technique are simple and require merely organization and supervision. They entail very little extra work on the part of the staff of a general hospital. The setting apart of one nurse in each ward to deal with all these tests would probably result in greater accuracy in the collection and timing of materials.

Summary of the Routine Methods.

1. The test is performed in the morning on the fasting patient at rest. It has been shown that kidney function is more constant at such times.
2. A "fasting" specimen of blood (five cubic centimetres) is collected for the estimation of the urea content. This is not necessary for the clearance test, but it gives a useful comparison with old standards and also indicates the degree of rise in blood urea level after urea has been given by mouth.
3. The bladder is emptied, if necessary by catheterization.
4. Fifteen grammes of urea in 120 cubic centimetres of water are given. The solution may be flavoured with one drachm of *Tinctura Aurantii*.
5. The exact time is noted.
6. Urine is collected at the end of the first hour. The time is noted.
7. Blood is collected for a second blood urea test one hour and forty-five minutes after the giving of urea by mouth. Fowweather has shown that the average level of blood urea is constant throughout the second hour, and specimens removed at any time in that hour show negligible variation. In a paper shortly to be published I shall confirm these findings.
8. A second specimen of urine is collected two hours after the giving of urea. The exact time is noted.
9. A third specimen of urine may be collected at the end of three hours for the purposes of checking the urea concentration and determining the amount excreted in three hours. This, however, is not essential.

The test therefore in its minimal requirements involves no extra work (the second and ninth steps may be eliminated), while a comparison with old standards involves only the taking of an extra specimen of blood for urea content estimation in the second hour.

The method adopted in this series for estimation of urea was the soya bean and aeration method of McClean, samples of three cubic centimetres of blood being used; the ammonia formed was drawn into N/100 sulphuric acid with methyl red as an indicator, and titrated against N/100 caustic soda. A number of blood samples could be aerated in series, the extra time taken being thus considerably reduced.

In all cases, chemical, physical and microscopic examination of the "fasting" urine was made.

As all tests were controlled by myself, opportunity was provided for collation of these findings with one another and with the clinical history.

The Nomographic Chart.

The figures obtained were subjected to detailed mathematical analysis by Dr. M. Barnard, and in the search for a simple procedure to eliminate the use of square root calculations a nomographic chart was evolved (Figure 1). The legend explains its method of use.

Volume of urine (*U*), blood urea content (*B*) and urea concentration (*V*) are represented on perpendicular lines, and the point at which a line joining the known values of *U* and *B* crosses the central vertical line is first determined, say *X*. This point *X* is then connected with that point on the line *V*, which represents the known volume of urine excreted per minute. Extension of this last line to line *C*, which is divided into percentage clearance values, allows a direct reading of the clearance as percentage value of normal function (72%). For purposes of simplification, figures above 100% have been excluded and would be given as "above 100%", which is adequate for clinical purposes. Likewise the lowest value has been set at 10%. Values for urea concentration on the chart lie between 0·5 gramme *per centum* and 4·0 grammes *per centum*, and volumes of urine excreted per minute lie between 0·1 cubic centimetre and 4·0 cubic centimetres. It was considered that these figures represented the extreme limits likely to be met with in clinical work.

It should be noted that the vertical lines of the nomograph are divided in logarithmic scale, and hence the scale markings are of variable value. If the nomograph is read from above downwards, the values are as follows:

On *V* line:
- With values from 0·1 to 0·2, each division = 0·02
- With values from 0·2 to 1·0, each division = 0·05
- With values from 1·0 to 4·0, each division = 0·2

On *B* line:
- With values from 10 to 50, each division = 2·0
- With values from 50 to 100, each division = 5·0
- With values from 100 to 250, each division = 10·0

On *U* line:
- With values from 0·5 to 1·0, each division = 0·02
- With values from 1·0 to 4·0, each division = 0·1

On *C* line:
- With values from 10 to 20, each division = 0·5
- With values from 20 to 50, each division = 1·0
- With values from 50 to 100, each division = 2·0

The chart will shortly be made available in compact form for general use.

ANALYSIS OF RESULTS.

In determining the significance of the clearance test in relationship to other tests of renal function, it will be convenient to collect the results into the following groups: group A, in which all tests give normal results; group B, in which all tests give poor results; group C, in which the results of certain tests are at variance. In group A little trouble will arise as to the true assessment of the kidney condition. In group B, in which all results are poor, the advantage of one test over another may be the ability to determine by the clearance test the quantitative degree of poorness of renal function. In group C, divergence of results may be expected and the final determination of the state of renal function may present many difficulties.

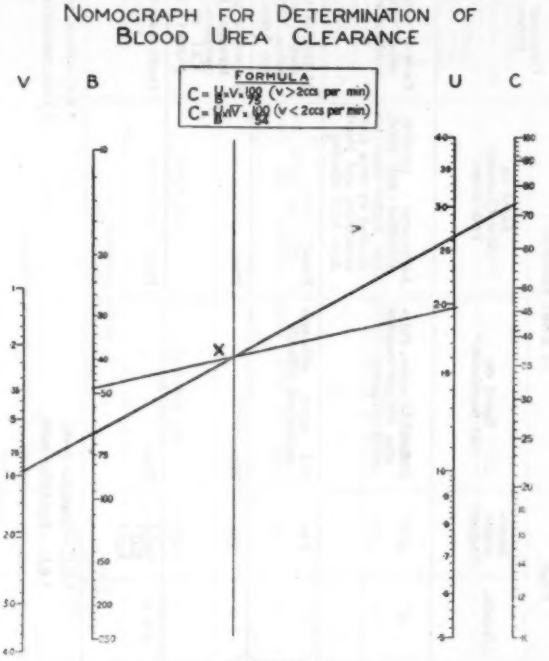


FIGURE I.

V = volume of urine excreted in cubic centimetres per minute; *U* = urea concentration (grammes of urea per 100 cubic centimetres of urine); *B* = blood urea level (milligrammes of urea per 100 cubic centimetres of blood); *C* = blood urea clearance as a percentage of the normal value. To determine *C*, place a straight edge through values of *U* and *B*; note point of intersection with central unscaled line; then place straight edge through this point and value of *V*. The point of intersection of this line with the *C* scale gives the value of *C*. Note: *U* is plotted on the nomograph in grammes *per centum*; in the formula it is expressed in milligrammes *per centum*.

Arbitrary Standards.

In arriving at standards of normality or poorness of renal activity, it would be impossible to satisfy all criticisms; borderline cases will continually crop up, which may possibly barely fall into their particular group. However, it should be remembered that we are dealing with a comparison of cases, and therefore figures are intended to be of relative rather than of absolute value. In the final evaluation, no single result is intended to replace the total conception of the case, and no single finding can be regarded as of absolute or pathognomonic significance.

In group A we shall take as normal the following figures: (i) a fasting blood urea level under 40 milligrammes per 100 cubic centimetres; (ii) a second-hour urea concentration of over 1·5 grammes; (iii) a urea clearance of over 80%.

In group B we shall take as poor the following figures: (i) a fasting blood urea level of over 40 milligrammes per 100 cubic centimetres; (ii) a second-hour urea concentration under 1·5 grammes; (iii) a urea clearance of under 70%. A clearance value of between 70% and 80% is to be regarded as indicating moderate impairment of renal function.

In group C, if the figures for normal and poor results are accepted with reservation, a number of subjects will give normal results to tests of one type and poor results to tests of another type, and considerable divergence may occur. To assess the comparative value of the clearance test against others, we shall divide these cases into categories as follows: (i) good clearance—over 80%; (ii) impaired clearance—70% to 80%; (iii) poor clearance —under 70%.

The detailed analysis of each of these groups according to its point of variation will be carried out in the latter part of this paper. Tables I to V give in detail the results obtained.

Group A: All Results Normal.

In group A there are 17 cases (Table I). Space will not permit inclusion of all, and only two examples are given in Table I. No great difficulty arises, and little comment need be made, except to state that in no case in which clearance was over 80% was the urea concentration in the second hour under 1·5 grammes per 100 cubic centimetres, or the fasting blood urea level over 40 milligrammes per 100 cubic centimetres. Follow-up of all these cases revealed that the biochemical assessment was accurate, and the clearance figure therefore gave a true indication of renal activity. That this could not be said of urea concentration tests and blood urea estimations alone will be seen from review of group C, subgroup 3*a* (Table IV).

Group B: All Results Poor.

In group B, as in group A, there is no great difficulty, for all tests reveal a damaged kidney (Table II). However, the ability to assess the degree of damage or impairment is possible only with the clearance test. This quantitative estimation of renal activity allows the determination of progress in a given case, and by its use a much more accurate prognosis may be given.

Of the seven sets of results falling into this group, I shall select those that illustrate particularly well the quantitative value of the clearance figure.

CASE VIII.—A male patient, aged seventy-two years, suffered recently from giddy turns and headache. Urea concentrations of 0·5 gramme and 1·2 grammes per 100 cubic centimetres and a blood urea level of 44 milligrammes per 100 cubic centimetres revealed renal impairment, the degree of which was difficult to assess. The urea clearance figure of 58% suggested some impairment of renal function, but not of gross type. In association with other circumstances the symptoms were therefore regarded as more essentially vascular and hypertensive than renal. Four years later the patient maintains reasonable health, confirming this point. (See also comment on problem of age at the end of this paper.)

CASE XI.—A male patient, aged fifty-eight years, whose health had recently been failing, had better urea concentration than the patient in Case VIII (1·5, 1·3 grammes per 100 cubic centimetres); but he had a blood urea level of 54 milligrammes per 100 cubic centimetres. Without clearance figures the degree of difference between this and the previous case could not be accurately determined. However, a urea clearance of 36%, as compared to 58%, allowed a clear distinction between the cases. A bad prognosis given in this instance was confirmed by the report of the patient's death five months later.

With regard to Case XXI (ii), the findings are the results of a second series of tests performed on an elderly patient suffering from prostatic enlargement. Recent retention of urine had occurred, and hence the results show very little quantitative improvement from the previous tests (Case XXI (i)). Later, although the blood urea level and the urea concentration were of a similar order (Case XXI (iii), Table V), the urea clearance figure was 72%, which was in keeping with the patient's clinical improvement. Prostatectomy was successfully performed at this stage. The change in his condition from "unsafe" to "safe risk" was indicated by the clearance figures alone, other tests being of little value.

CASE XXIII.—A male patient, aged thirty-seven years, over a period of two years insidiously developed œdema and

TABLE I.

Group A. All Results Normal.

Case Number.	Volume of Urine. (Cubic Centimetres.)		Urea Concentration. (Grammes per 100 Cubic Centimetres.)		Blood Urea Level. (Milligrammes per 100 Cubic Centimetres.)		Clearance as Percentage.	Examination of Fasting Urine.		Biochemical Assessment of Renal Function.		Comment and Follow-up.	Ultimate Assessment Based on all Factors.
	First Hour.	Second Hour.	First Hour.	Second Hour.	Before Giving of Urea.	After Giving of Urea.		Albumin.	Microscopic Findings.	Based on Old Standards.[6]	Based on New Clearance Test Alone.[7]		
XIX	138	96	2·0	3·1	27	46	158	0[1]	Nil.	Excellent.	Excellent.	Previously an albuminuria of pregnancy.	Satisfactory.
XXXIV	90	70	2·8	2·9	36	56	100	0	r.b.c.[2]	Good.	Good.	Healthy male. Routine tests.	Good function.

[1] 0 = No albumin.

[2] r.b.c. = Red blood corpuscles.

[6] Urea concentration, blood urea level.

TABLE II.

Group B. All Results Poor.

Case Number.	Volume of Urine. (Cubic Centimetres.)		Urea Concentration. (Grammes per 100 Cubic Centimetres.)		Blood Urea Level. (Milligrammes per 100 Cubic Centimetres.)		Clearance as Percentage.	Examination of Fasting Urine.		Biochemical Assessment of Renal Function.		Comment and Follow-up.	Ultimate Assessment Based on all Factors.
	First Hour.	Second Hour.	First Hour.	Second Hour.	Before Giving of Urea.	After Giving of Urea.		Albumin.	Microscopic Findings.	Based on Old Standards.[7]	Based on New Clearance Test Alone.		
VIII	310	190	0·5	1·2	44	92	58	0[1]	H.C.[3]	Difficult to assess. Polyuria nullifies concentration figures.	Assessment possible. Function not good, but better than indicated by urea concentration and blood urea level (fasting).	Patient remains well under conditions of minimal strain.	Essentially hypertensive.
XI	130	114	1·5	1·3	54	92	36	+[2]	Pus.	Not good, although assessment difficult.	Poor.	At time of test patient noticed severe headaches. Hypertension was found.	Poor kidney. Confirmed by death shortly afterwards.
XXI (ii)	170	174	0·82	1·2	67	136	34	++	Pus.	Poor.	Poor.	Second of tests to determine fitness for operation. (See Case XXI (i) and (iii), group C, Table V.)	—
XXIII	68	52	0·6	0·77	210	250	5	+++	G.C.[4] E.C.[5] B.C.[6]	Poor.	Poor.	Death three weeks later.	Clearance gives assessment of amount of renal activity; autopsy confirms findings.

[1] 0 = No albumin.

[2] + = Albumin present.

[3] H.C. = Hyaline casts.

[4] G.C. = Granular cysts.

[5] E.C. = Epithelial casts.

[6] B.C. = Blood casts.

[7] Urea concentration, blood urea level.

TABLE III.

Group C. Results at Variance. Subgroup 2. Urea Clearance Impaired.

Case Number.	Volume of Urine. (Cubic Centimetres.)		Urea Concentration. (Grammes per 100 Cubic Centimetres.)		Blood Urea Level. (Milligrammes per 100 Cubic Centimetres.)		Clearance as Percentage.	Examination of Fasting Urine.		Biochemical Assesment of Renal Function.		Comment and Follow-up.	Ultimate Assesment Based on all Factors.
	First Hour.	Second Hour.	First Hour.	Second Hour.	Before Giving of Urea.	After Giving of Urea.		Albumin.	Microscopic Findings.	Based on Old Standards.[1]	Based on New Clearance Test Alone.		
(a) Other Results Normal.													
III (ii)	212	126	1·2	2·0	37	67	77	0[1]	Nil.	Fair to good renal function.	Impaired, but much improved since previous test.	(See Case III (i), Table V.) Patient clinically is better and no further attacks of hypertensive encephalopathy.	Prognosis given from Case III (i) is upheld by these later results and shows a satisfactory state.
V (i)	86	80	2·5	2·5	20	72	72	0	Pus.	Very good. No means of assessing damage.	Fair. Some renal damage indicated.	Polyuria persisted and became worse at time of second test. (See Case V (ii).) Albumin found in urine and blood pressure became elevated.	Clinical assessment agreed with clearance figures in second test (Case V (ii)). (See group C, subgroup 3a, Table IV.)
XXX (ii)	106	70	2·8	3·43	38	85	71	++[2]	G.C.[3]	Good.	Impaired.	An albuminuric in otherwise good health.	Casts reveal some renal damage and clearance confirms. (See Case XXX (i).)
(b) Blood Urea Level Alone Elevated.													
XV	150	95	2·2	2·6	42	85	72	0	Nil.	Fair; blood urea level, a little elevated.	Impaired.	Hypertension. Headaches. Cerebral spasms. Some time later coronary thrombosis.	Symptoms better accounted for on vascular basis as suggested by test results.
(c) Concentration Alone Poor.													
XIII	128	120	1·0	1·0	16	35	76	+++	Nil.	Poor concentration, although blood urea level good. Assessment difficult.	Clearance better than indicated by urea concentration. Prognosis favourable.	History of insidious oedema and albuminuria. Well after four months' treatment and now has no evidence of past renal condition.	Better prognosis confirmed.

[1] 0 = No albumin. [2] + = Albumin present. [3] G.C. = Granular casts. [4] Urea concentration, blood urea level.

albuminuria of symptomless type suggesting a nephrosis. He began gradually to suffer from anorexia and from the need to micturate during the night, at first insufficient to keep him from work. Later failing vision and hypertensive and retinal changes left no doubt that chronic renal disease was present. The urea concentration, blood urea level and urea clearance figures all revealed severe kidney damage, and since the urine contained casts, red blood corpuscles and albumin, a grave prognosis was given. The extreme gravity of the case, suggested on clinical grounds, was amply confirmed by biochemical tests and finally and accurately by the urea clearance result of 5%. Three weeks later the patient developed uræmic coma and died.

Space will not permit publication of the remaining cases in this group.

Group C: Results at Variance.

In group C there are three subgroups: (i) results showing good clearance, (ii) results showing impaired clearance, (iii) results showing poor clearance.

Subgroup 1: Results Showing Good Clearance (Values over 80%).—The results in this subgroup are of theoretical significance only, for in no case in which the clearance value was over 80% was impairment of renal function indicated by any other test. This of itself shows the value of the clearance figure. The converse is not true, for in a number of cases in which poor clearance results were obtained, other tests produced normal results (Table IV, subgroup 3a).

Subgroup 2: Results Showing Impaired Clearance (Values from 70% to 80%).—In the interpretation of results showing slight impairment of renal function, the following points should be remembered: (i) The deficiency being slight, very little clinical evidence may be found to confirm it. (ii) The kidney at the time of the test may be in a

state of transition, either toward improvement or toward deterioration. (iii) The rapidity of development of the lesion may influence the clinical condition seen. Thus an insidiously developing state may produce very few symptoms, while a rapidly progressive condition may present a different picture. Each type may be associated with similar biochemical findings. (iv) Age must be taken into account in the slighter degrees of renal failure. A youth having only 70% of renal function would be in a worse category than an elderly patient giving the same results to tests.

The following are the possible variations of results of the other tests of this group: (*a*) normal blood urea level and urea concentration; (*b*) elevated blood urea level alone; (*c*) poor urea concentration alone; (*d*) elevated blood urea level, poor urea concentration.

Subgroup 2a.—In each of six tests a normal blood urea level and urea concentration were revealed, but impaired urea clearance was found (Table III).

With regard to Case III (ii), the results are those of the second series of tests carried out on a male patient, aged sixty-four years. The original test (Case III (i), Table V) showed a urea clearance value of 60%. At that time a history of recurrent cerebral seizures was given, and hypertension with albuminuria was found. With treatment the attacks ceased, and the second test (Case III (ii)) revealed a urea clearance of 77%. Follow-up examination four years later again showed the patient to be still free of his cerebral seizures and comparatively well. The improvement in the patient's condition, which could be assessed from the clearance figures, could not have been determined by other tests, the results of which were of the same order throughout.

CASE V (i).—A female patient, aged forty-one years, with pyuria, had normal blood urea level and urea concentration. A urea clearance value of 72% revealed impaired kidney function, and further review two years later revealed increased pyuria, albuminuria and hypertension, with further impairment of renal function.

The first clearance test therefore gave a truer indication of renal function than did the misleading normal results to other tests.

In Case XXX (ii) the patient, a young male, who gave otherwise good results to tests, had impairment of renal function compatible with the presence of albuminuria and casts. The other results obtained at this time were of a similar order to those obtained some six weeks before; but the clearance figure was lower. This may indicate that the clearance test alone would reveal progress of the kidney condition.

Cases VI, XXXIX and XLI provide further examples of this group not included here.

Subgroup 2b: Impaired Clearance; Blood Urea Level Alone Elevated, Urea Concentration Normal.—In Case XV a male patient, aged fifty-eight years, suffering from recurrent cerebral seizures, gave satisfactory results to the urea concentration test; but his blood urea level was slightly elevated (42 milligrammes per 100 cubic centimetres). The urea clearance value of 72% gave a quantitative estimation of the renal function, suggesting a minor degree of renal impairment, and the symptoms could therefore be regarded as of a vascular nature. Two years later the patient suffered from a coronary thrombosis, from which ultimate recovery took place. This ability to identify the pure hypertensive from the renal hypertensive may prove to be one of the most valuable uses of the urea clearance test.

Case XXX (i), already discussed, is a further case in this group.

Subgroup 2: Impaired Clearance Value; Urea Concentration Alone Poor; Blood Urea Level Normal.—In Case XIII a female patient, aged eighteen years, gave a history of insidiously developing œdema and gross albuminuria. There were no elevation of blood pressure and no casts or red blood corpuscles in the urine. While these findings pointed to a degenerative or nephrotic lesion, the urea concentrations of 1·0 gramme for each hour made interpretation difficult. The clearance figure of 76% suggested a good prognosis, and with adequate treatment the patient's urine proved to be free of albumin after six months. This improvement was maintained, and two years later tests of the urine after severe exercise revealed no trace of albumin. The patient still remains well.

There were no cases in this group (slight impairment of urea clearance) in which elevation of blood urea level and poor urea concentration were found.

Subgroup 3: Poor Clearance Values (Under 70%).—In subgroup 3 of group C, other results at variance with the urea clearance values were: (*a*) normal blood urea level, normal urea concentration; (*b*) blood urea level alone elevated; (*c*) urea concentration alone poor.

Subgroup 3a: Poor Urea Clearance; Other Results Normal.—In general, it may be said that the findings in this group make biochemical assessment a matter of difficulty (Table IV). The blood urea level and urea concentration being normal, the poor clearance figure required careful checking. A review of the following cases will show that the urea clearance test alone of all others gives the truest estimation of the state of the kidney. Many results, which previously would have been taken to indicate normal renal function, are thus to be interpreted very differently. Of the 19 cases that fall into this subgroup, five will be selected to illustrate most clearly the true interpretative value of the urea clearance test against other tests.

CASE VII.—A patient who presented excellent concentrating power of the kidney and a blood urea level of 39 milligrammes per 100 cubic centimetres had some albumin and casts in the urine. There would be little indication of impaired renal activity from the urea concentration tests or blood urea level; the urea clearance test, however, revealed only 53% of renal activity. A bad prognosis could therefore be given from the urea clearance test alone. That this was correct was proven by follow-up of the patient, when it was learned that death occurred five months later from uræmia.

CASE IX.—A patient, aged forty-five years, gave a history of dysuria and renal pain. Urea concentrations of 2·3 and 2·9 grammes per 100 cubic centimetres for first and second hours respectively, with a blood urea level of 28 milligrammes per 100 cubic centimetres, indicated a very satisfactory renal function according to the old standards. The urea clearance, however, proved to be 45%—a poor result. Follow-up revealed that after the test X-ray examination of the kidneys revealed a right renal calculus (the right kidney proving functionless when "Uroselectan" was injected), and also a small left renal calculus; 45% of renal activity would be a close approximation to the amount of active kidney tissue in this patient. The inability of the kidney to deal with the urea is at once recognized by the rise of the blood urea level from 28 to 171 milligrammes per 100 cubic centimetres, after 15 grammes of urea had been given by mouth. Only the clearance test (after the kidney had been subjected to strain) could have revealed this defect.

CASE XII.—A patient whose urine contained albumin had a urea concentration which on our relative standards was designated "normal" (1·5, 1·6 grammes for the first and second hours respectively), and also a blood urea level of 38 milligrammes per 100 cubic centimetres. Again, after urea had been given by mouth, the blood urea level rose sharply to 90 milligrammes per 100 cubic centimetres; this produced a lowering of the urea clearance value to 34% renal function. According to old standards, no biochemical evidence of renal failure existed; but the urea clearance figure caused a bad prognosis to be given. This was confirmed from the further progress of the patient, who died five months later from renal failure.

CASE XXVIII.—A patient requiring prostatectomy had urea concentrations of 1·5 and 2·2 grammes per 100 cubic centimetres for the first and second hours, with blood urea level of 32 milligrammes per 100 cubic centimetres of blood. These figures would be considered very satisfactory according to old standards; but the urea clearance value of 59% was just below the limit of safety for prostatectomy and revealed the possibility of danger. Ten days after operation the patient died from anuria and renal failure.

CASE XXXII.—Case XXXII is of similar significance to Case XXVIII. A patient requiring prostatectomy had a urea clearance value of 55% in spite of good urea concentration figures (tests for the fasting blood urea level were not performed). Again, death occurred ten days after prostatectomy.

TABLE IV.

Group C. Results at Variance. Subgroup 3. Poor Urea Clearance.

Case Number.	Volume of Urine. (Cubic Centimetres.)		Urea Concentration. (Grammes per 100 Cubic Centimetres.)		Blood Urea Level. (Milligrammes per 100 Cubic Centimetres.)		Clearance as Percentage.	Examination of Fasting Urine.		Biochemical Assessment of Renal Function.		Comment and Follow-up.	Ultimate Assessment Based on all Factors.
	First Hour.	Second Hour.	First Hour.	Second Hour.	Before Giving of Urea.	After Giving of Urea.		Albumin.	Microscopic Findings.	Based on Old Standards.[4]	Based on New Clearance Test Alone.		
(c) Other Results Normal.													
V (ii)	52	48	2·8	2·9	38	58	57	+[1]	Pus.	Good. Better concentration power than previously.	Poorer function than previously.	Second of tests. (See Table III.)	Shows progressive condition.
VII	40	26	2·7	2·8	39	64	53	++	E.C.[2] L.C.[3]	Good renal function. No conception that renal inefficiency is present.	Poor.	Bad prognosis given. Patient died five months later (uræmia).	Clearance test alone gave true prognosis.
IX	58	120	2·3	2·9	28	171	45	+	Pus.	Very good.	Poor. Advised against operation.	A stone in right kidney, from which no "Uro-selectan" was excreted, also a left renal calculus.	Old and new standards greatly at variance. Clearance result confirmed by later findings.
XII	72	66	1·5	1·6	38	90	34	++	G.C.[4] E.C.	Not good, but not severe impairment.	Severe impairment of renal function. Bad prognosis given.	Patient died five months later. Renal failure.	Severe impairment confirmed.
XXVIII	84	60	1·5	2·2	32	68	60	+	Pus.	Good.	Poor risk.	Died 10 days after operation.	Borderline case. Tests revealed risk, no help by clinical appearance alone.
XXIX (i)	86	90	1·6	1·6	35	59	65	++	G.C. E.C.	Good.	Impaired.	With tests performed over a two-year period, the figures reveal almost identical results.	Similar results over a long period. Clinical condition unaltered.
XXIX (ii)	38	56	2·5	2·1	38	57	61	++	G.C. E.C.	Good.	Impaired.		
XXIX (iii)	116	78	1·8	1·8	36	59	65	++	H.C.[5] G.C.	Good.	Impaired.		
XXXII	72	96	1·5	1·8	—	75	55	+	Pus.	Fairly satisfactory.	Poor risk.	Death 10 days after prostatectomy.	Clearance test revealed dangers of operation.

[1] + = Albumin present.
[2] E.C. = Epithelial casts.
[3] L.C. = Leucocytic casts.
[4] G.C. = Granular casts.
[5] H.C. = Hyaline casts.
[6] Urea concentration, blood urea level.

Subgroup 3b: Poor Urea Clearance Value, Elevated Blood Urea Level, but Good Urea Concentration.—It has been stated that an elevated blood urea level alone is a significant indication of poor kidney function; but its true interpretation can be made only in the light of all other facts (Table V). By the urea clearance test, it is possible to determine the value of an elevated blood urea level in relationship to prognosis.

The results in Case III (i) are the results of the first two tests carried out on an elderly male patient. The fasting blood urea level of 55 milligrammes per 100 cubic centimetres of blood would indicate considerable renal damage. The urea concentration, however, was good. The urea clearance value of 60% in this first test therefore was interpreted as a better total result than might have been expected from the blood urea level alone, and a better prognosis was given. The prognostic significance of the first clearance test was confirmed by the finding of considerable improvement three years later —a normal blood urea level and 77% urea clearance (Case III (ii), Table III).

With regard to Case XLIX, a blood urea level of 46 milligrammes per 100 cubic centimetres may have been misleading in a case for prostatectomy; but the urea concentration was satisfactory (2·8, 3·2 grammes for the first and second hours) and the urea clearance value was 69%. So the operation was recommended with confidence, and was successfully carried out.

With regard to Case LIV, a urea clearance value of 55% suggested some risk from prostatectomy for a patient who otherwise had good concentrations. No estimation of the fasting blood urea level was made, but the blood urea level after urea had been taken by mouth was 74 milligrammes per 100 cubic centimetres. The risk indicated by the clearance figure was substantiated by subsequent events; death occurred shortly after operation.

Subgroup 3c: Poor Clearance, Poor Urea Concentration, Good Blood Urea Level.—In Case IV, a patient, aged forty-five years, had a normal blood urea level (33 milligrammes per 100 cubic centimetres) and urea concentrations of 1·0 and 1·5 grammes for the first and second hours of the urea concentration test. The clearance value of 52% was confirmed in a remarkable quantitative fashion by the finding, at operation, of a gross unilateral pyonephrosis.

The results in Case XXI (i) and Case XXI (iii) are those of the first and third of two tests carried out on a patient who was to have

TABLE V.

Group C. Results at Variance. Subgroup 5. Poor Urea Clearance.

Case Number.	Volume of Urine. (Cubic Centimetres.)		Urea Concentration. (Grammes per 100 Cubic Centimetres.)		Blood Urea Level. (Milligrammes per 100 Cubic Centimetres.)		Clearance as Percentage.	Examination of Fasting Urine.		Biochemical Assessment of Renal Function.		Comment and Follow-up.	Ultimate Assessment Based on all Factors.
	First Hour.	Second Hour.	First Hour.	Second Hour.	Before Giving of Urea.	After Giving of Urea.		Albumin.	Microscopic Findings.	Based on Old Standards.[1]	Based on New Clearance Test Alone.		
(b) Blood Urea Level Alone Elevated.													
III (i)	90	95	2·1	2·3	55	85	60	+[1]	Nil.	Difficult, because good and concentration elevated blood urea level. Probably regard as fair.	Better than elevated blood urea alone would indicate.	Case III (i) reveals good clearance figures in comparison to blood urea, and with good concentration findings meant good prognosis.	Confirmed by later finding. (See Case III (ii), Table III.) Patient well five years later.
XLIX	47	49	2·8	3·2	46	77	69	+	Pus.	Fair to good.	Good.	Prostatectomy successful. Fasting blood urea level might have been misleading.	Satisfactory function confirmed.
LIV	72	96	1·5	1·8	—	74	55	+	Pus.	Fair.	Poor.	Death shortly after operation.	Risk revealed by clearance test.
(c) Urea Concentration Alone Poor.													
IV	92	118	1·0	1·5	33	74	52	+	Pus.	Poor concentration suggests poor function, although no elevation of blood urea level.	A more precise idea of renal activity is possible.	Operation revealed one kidney entirely functionless— gross unilateral pyonephrosis.	Urea clearance of quantitative significance— apparently accurate.
XXI (i)	58	104	0·9	0·9	26	70	31	++		Poor function, although good blood urea level.	Poor.	Immediately after retention of urine (Case XXI (i)) and some weeks later (Case XXI (ii), group B) poor renal function. With treatment considerable recovery occurred; patient finally fit for operation. This was successful, and patient is now well.	Blood urea level and urea concentration of similar order throughout. Urea clearance alone revealed improvement.
XXI (iii)	96	224	0·56	0·71	35	49	72			Fair to poor.	Impaired, but much improved.		

[1] + = Albumin present.

[2] Urea concentration, blood urea level.

a prostatectomy. The first was carried out soon after an attack of acute retention of urine, and the urea clearance figure of 31% was in keeping with his poor clinical condition and suggested that the patient at that time was unfit for operation. Three months later clinical improvement occurred, and although the results of tests on the usual standards of blood urea level and urea concentration were of a similar order to those of the first test, the urea clearance was greatly improved (72%). Prostatectomy was successfully performed at this stage. The biochemical assessment of improvement was able to be made from the results of the urea clearance test alone (see Table V).

DISCUSSION.

Kidney function tests have been performed in 67 instances in a series of 54 cases, and a comparison has been made between urea clearance on the one hand and urea concentrations and blood urea level on the other, and the clinical condition.

Theoretical and practical considerations having been dealt with, the necessity to give urea by mouth in the estimation of the clearance was established; the particular test applied here was based on the principle that for adequate and complete assessment of renal activity, the kidney must be subjected to a test involving stress akin to what may be demanded of it by operation or the like. Frequently, when the results of simple blood urea estimations and urea concentration tests were normal, the urea clearance test, after 15 grammes of urea had been given by mouth, revealed considerable renal defect. Table IV depicts these results, and it will be seen that in this group the clearance figures were the only ones to give a true estimation of prognosis. Kidney damage must be fairly advanced before the blood urea level becomes elevated, and likewise the results of urea concentration tests will be misleading if volumes are to be ignored or only casually regarded. The urea clearance test, by taking into consideration the influence of one on the other, allows the more accurate assessment of renal reserve power and therefore prognosis.

It hardly needs emphasis that figures can have their

full meaning only when interpreted in the light of other relevant details. It would be as unfair to expect assessment of the true condition of the kidney from any one single result as it would be to determine the state of the heart from the apex beat alone. Just as in the latter case radiography and electrocardiography are necessary, so in kidney conditions laboratory findings are to be considered in the reflected light of clinical data, not in the more brilliant yet less penetrating glare of direct mathematical investigation. The minimum requirements additional to the results of the urea clearance test would be an adequate clinical history, estimations of blood pressure, detailed examination of the urine (physical, chemical and microscopic), and examination of the fundi. Fowweather's[10] statement is a fair summary of this view:

> The clinical laboratory should never be regarded as an institution which of itself is capable of supplying a diagnosis. It is a means of obtaining additional information about a patient where it is felt other information is needed. A diagnosis must then be made in the light of all clinical evidence available.

The Nomographic Chart.

In order better to satisfy these criteria and so to allow the physician to determine the urea clearance from figures (themselves of independent value) such as the blood urea level, the urea concentration and the volume of urine excreted per minute, a simple nomographic chart has been devised (Figure I). This eliminates all mathematical formulæ. Being of small size, it can be readily used at the bedside, and it greatly simplifies the determination of the final result. The chart shows in graphic fashion that for volumes of urine about two cubic centimetres per minute, the use of either $\frac{UV}{B}$ or $\frac{U\sqrt{V}}{B}$ results in very little difference in clearance values. The figure 2 on the V line is represented by two separated divisions, the upper determined from formula $\frac{UV}{B}$, the lower from $\frac{U\sqrt{V}}{B}$. The projection of either through any point on the middle blank line to C would give the difference in clearance value from each formula.

From the chart many important points are to be noted. If the common average volume is taken at two cubic centimetres per minute, for a clearance of 80% the line joining V to C called XY (Figure II) must cross the blank at O. Any reduction in volume below two cubic centimetres per minute will strike the line C at a lower point, until for volumes of 0·5 cubic centimetre per minute the clearance result becomes 40%. A straight rule pivoting about O will give the values necessary for B and U to cross at O, and it will be seen that for average normal values of U, B and V this point would be the lowest crossing point on the blank line for normal clearance.

Again, to obtain an 80% clearance with volumes at their maximum (four cubic centimetres per minute), the blank line will be crossed at point N, which will therefore be regarded as the lowest possible crossing point for normal clearance results. Any crossing of the line joining B and U below N must always give a poor clearance result. O, then, represents the lowest crossing level for average normal results, N the absolute lowest crossing point for normal results. The point of crossing between O and N, while usually giving figures indicative of impaired clearance, will really vary with the volumes of urine obtained.

Factors Influencing the Prognostic Value of Clearance Results.

The Problem of Age.

It has already been stated that the isolated urea clearance figure must be supported by other clinical factors. The first of these is age. It may be assumed that age has the effect of equally reducing the reserve power of all organs, and that only when the balance of uniform reduction is upset does illness develop. Unless, therefore, the general state of the subject's reserves is known, it is not possible to place reliance on urea clearance figures alone. As an example, let us take Case VII, in which the urea clearance was 53%, and Case VIII, in which it was 58%. The former patient was a young male, with a history of rapid failure of health, the latter a man, aged seventy-two years, with insidiously developing symptoms. While the older patient has had time for numerous compensating mechanisms to come into play, the younger man has not. To base conclusions on urea clearance figures alone would therefore be misleading.

NOMOGRAPH FOR DETERMINATION OF BLOOD UREA CLEARANCE

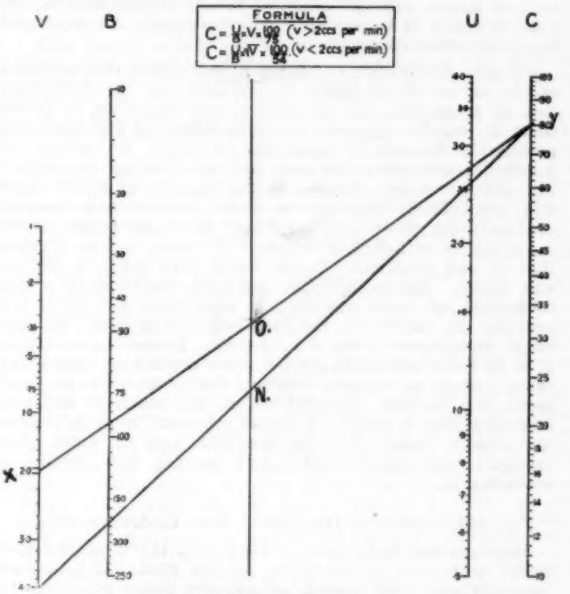


FIGURE II.

V = volume of urine excreted in cubic centimetres per minute; U = urea concentration (grammes of urea per 100 cubic centimetres of urine); B = blood urea level (milligrammes of urea per 100 cubic centimetres of blood); C = blood urea clearance as a percentage of the normal value. To determine C, place a straight edge through values of U and B; note point of intersection with central unscaled line; then place straight edge through this point and value of V. The point of intersection of this line with the C scale gives the value of C. Note: U is plotted on the nomograph in grammes *per centum*; in the formula it is expressed in milligrammes *per centum*.

The Lesion.

Acute Nephritis.—That results should be interpreted in conjunction with the clinical history is best seen in acute renal conditions. Here concentrating power and excretion are frequently maintained, and the blood urea level therefore is not greatly altered. Thus results of tests are usually better than the clinical condition would indicate. The explanation may lie in the fact that when disease strikes a previously healthy kidney, sufficient functional ability is retained by the renal units (or nephrons) to maintain adequate excretion. An additional possibility in some cases—pregnancy in particular—may be that an extrarenal factor is at work (for example, anti-diuretic hormone). Whatever the explanation, the degree of activity of the lesion must be taken into consideration when results are being interpreted. Case VII, in which the urea clearance was 53%, was associated with albumin and casts of epithelial and leucocytic variety in the urine, and the condition was therefore one of active nephritis; the urine in Case VIII, in which the urea clearance was 58%, contained no albumin and only hyaline casts. The urea clearance results alone do not indicate much difference in the outlook; but from the urinary findings the patient in Case VII had an active, possibly rapidly progressive lesion, and

the patient in Case VIII a slow, inactive, probably stabilised condition. The difference in prognosis was vindicated by the follow-up, for the patient in Case VII died five months later, and the patient in Case VIII remains in satisfactory health four years later. A further example is seen in Case XII, in which the urea clearance value was 34% and the urine contained "half albumin" and granular and epithelial casts; this is in contrast with Case XXI (i), in which, although the urea clearance was 31%, only gross pyuria was present. The former patient died in five months from renal failure, while in the same period the latter improved sufficiently to undergo operation. Urea clearance figures, therefore, cannot be regarded as of prognostic value without adequate determination of the type of lesion, and the simplest means of establishing the type of lesion is to examine microscopically a centrifuged early morning specimen of urine.

Chronic Nephritis.—It has been seen above that evidence of the nature of the lesion is necessary for the determination of prognosis. In cases of chronic nephritis, in which there is usually considerable impairment of concentrating power, the number of nephrons in action is usually the maximum available, and each has this limited concentrating power. Any reduction in the number of active units will immediately encroach on renal reserve, and lessened concentrating power will no longer be compensated by the excretion of satisfactory volumes of urine, and so a retention of end products (raised blood urea level *et cetera*) will ensue. While therefore the urea clearance is a true indication of renal activity, it still does not take into account the ability of the tissues to compensate for and adapt themselves to the altered state. Prognosis, therefore, is to be given guardedly, and it must depend on such extra-renal factors as dietetic control, ability to undergo treatment, rest periods *et cetera*, before the complete and final interpretation is made. A single test can never determine the precise trend of renal function, and in these cases repeated tests at intervals may be the only means of assessing it.

The Significance of the Actual Urea Clearance Figure.

Sufficient has been said to show that the urea clearance figure alone cannot be taken as the guide to prognosis. Nevertheless, with regard to patients being prepared for major genito-urinary operations, some useful general rules may be laid down.

Subjects with a urea clearance figure of under 60% have been shown to present a fair degree of risk in major genito-urinary surgery. To go further and say that this precludes operation entirely would be to go too far in any single case; it may, however, be a useful red light where that is needed. The figure 60% may be considered much too high in certain hands, particularly if the operation is carried out in stages; for example, for a second-stage prostatectomy, a urea clearance figure of 40% would probably be safe.

The ability to decide from the urea clearance test results whether a two-stage operation is wise reveals one of the truly useful purposes of the test. Even if in the light of further experience the margins of safety may have to be altered, the true value of the urea clearance test should not be affected by such a change.

The Relationship to Other Results.

Blood Urea Level, Urea Concentrations.—In group C of this series we find 19 cases in subgroup 3*a* (Table IV) in which the blood urea level and urea concentrations were normal, yet in which urea clearance was poor. Such patients often look well clinically, and one is apt to read into the normal urea concentration and blood urea level a better interpretation than really exists. Thus if certain biochemical results tend to confirm the clinical conception of the case, the more searching urea clearance figure is ignored. Careful analysis of this group, however, has shown that when great divergence exists between clinical assessment with blood urea level and urea concentration on the one hand, and urea clearance on the other, it is wise to err on the side of the latter. The patient who looks clinically well, yet who gives results to tests of the order outlined is well known; just such a patient has made the clinician distrust the biochemical results, for when assistance was required, on old standards none was forthcoming. These comments do not apply to the urea clearance test, which in this group not only confirms existing danger, but brings many latent or new features to light. The normal blood urea level and urea concentration in Case VII were entirely misleading; the true state was revealed completely by urea clearance results. Likewise in Case IX, in which the urea clearance figure was 45%, a normal blood urea level and urea concentration were present. In both these cases the subsequent course left no doubt as to the precision of the urea clearance figure.

Since, when the urea clearance value was good, not one patient of this series (all groups) showed abnormalities in other tests, it may be concluded that a normal blood urea level and urea concentration may mean either a good or bad state of renal function, and only the clearance test will decide which is present. A good urea clearance result, on the other hand, always means satisfactory renal activity, a bad result, poor kidney function.

Dye Excretion Tests.—In the determination of unilateral kidney function, the indigo-carmine dye test is of undoubted value. To use it, however, as the sole means of determining the operative risk in a given case may result in considerable curtailment of the number of subjects for operation. If from one kidney the dye appears in a different time from that taken by the other kidney, total renal activity is very difficult to assess. Furthermore, the necessity for cystoscopy limits the use of the indigo-carmine test. In the majority of cases it should be used as an adjuvant to the urea clearance test.

Urea Excretion Concentration Test of Krieger.—Krieger's urea excretion concentration test is of considerable value, but has the disadvantage that it does not take into consideration the blood urea level at the time of the test, and it does not give the same precision in results nor the fluctuations of a case as are given by the urea clearance test. It requires three hours for collection of specimens, and in general it is a useful check when such three-hour samples are collected.

Summary.

1. The urea clearance test has been correlated with clinical and other findings in 54 cases involving 67 tests. By comparison with other tests and by follow-up investigation of clinical histories, a careful estimation of the value of the test has been made possible.

2. The importance of giving urea by mouth to subject the kidney to load or stress is emphasized. The simple Van Slyke test, by omitting this factor, is of less value than the modified urea clearance test here described.

3. It is believed that in cases in which the test is tried sporadically, technical errors such as inaccuracy of timing and collection of incomplete volumes of urine are the cause of failure of accurate results.

4. Emphasis is laid on the necessity for finally considering all aspects of the case before reaching a conclusion.

5. In this regard, a simple nomographic chart has been presented which will allow the clinician to determine from all available data the true urea clearance value. This eliminates all mathematical formulæ.

6. By repeated tests, the trend of a case is followed and an accurate prognosis is made.

Conclusions.

1. Results show that the urea clearance test is reliable and accurate and in many cases provides the only guide to renal damage. Because other means of biochemical assessment often prove misleading, it is urged that older methods should be discarded in favour of the routine use of the urea clearance test, and that this test should be seriously taken into consideration in assessment of prognosis or of fitness of a patient for operation.

2. The test appears to be of great value in cases of chronic nephritis and prostatic enlargement. Frequently in these cases, the urea concentration and blood urea level

are of little significance and are often dangerously misleading.

3. The increase in blood urea level two hours after urea has been given by mouth is a useful additional guide to the amount of renal reserve power, and as such it is of value in assessment of the operative risk in genito-urinary surgery.

4. It is considered that the urea clearance test, as an accurate and useful additional test of renal function, should be used as a routine method in all cases.

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I should like to express my indebtedness to Dr. M. Barnard, of the Forest Products Division of the Council for Scientific and Industrial Research, for the useful and extremely painstaking assistance she rendered me in the development of the nomographic chart, and to Mr. Whitehead for his fine line drawing of it; also to Professor P. MacCallam, of the pathology department of the University of Melbourne, for his interest at all times, to Dr. A. B. Corkhill, Director of the Baker Institute, Alfred Hospital, Melbourne, and to Dr. V. I. Krieger; finally, to the many private practitioners who assisted in the follow-up of patients. The major part of the work of this paper was assisted by a grant from the University of Melbourne General Research Fund. Delay in publication, unavoidable in present times of stress, is regretted.

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Reviews.

INFLUENZA.

THE fourth monograph in the series from the Walter and Eliza Hall Institute of Research in Pathology and Medicine is "a survey of the last fifty years in the light of modern work on the virus of epidemic influenza".[1]

It is only nine years since the introduction of the ferret to the experimental laboratory opened the way for the isolation of the long-suspected virus, and remarkable advances have taken place since then. Burnet's own use of the developing egg for primary isolation, and Hirst's discovery of the ability of the virus to clump red cells of the hen have replaced long and tedious mouse tests by exact and easily controlled laboratory procedures. The observations made upon small epidemics of the disease and on the levels of serum antibodies before and after these epidemics, have provided evidence for this survey, which now gathers the recent experimental work and suggests new lines of investigation. The occurrence of two major pandemics during the period under review, and the possibility of another in the future, have moulded the plan on which the monograph is prepared.

The description of the virus itself and its effects upon laboratory animals is the introduction to a masterly chapter in which the authors discuss human influenza as an ecological problem. The interesting section on the presence of virus in secretions and its transfer from person to person, on evidence relating to a virus-inactivating factor other than antibody in nasal secretions, and on the persistence of virus in situations other than the customary one in ciliated mucous membranes, leads to a consideration of antibody levels in the inter-epidemic period, and their significance and changes when the virus spreads. Burnet and Clark never lose sight of the fact that 75% of the population do not develop clinical disease, however prevalent the virus, and seek its explanation while investigating the effects shown by the other 25%.

An intimate knowledge of the strains isolated since 1933 and their behaviour permits an interpretation of the assembly of known facts about the pandemics of 1889-1891 and 1918-1919. The change in age group mortality and incidence, the failure of the first wave to produce immunization against a second, and the abnormal rapidity with which lesions of the respiratory tract developed, lead to the suggestion that the virus or viruses prevalent suffered a mutation or mutations bound up with the rapid transfer through human hosts, made possible by troop movements in time of war, and that those mutations may have included an added ability to infect alveolar as well as ciliated epithelium.

The final chapter shapes the evidence of the last ten years with the information of the previous forty into a plan for the future investigation of the disease. Quarantine, vaccination, both by virus and by secondary bacterial invaders, and the large-scale measures for their application, are discussed in detail. Burnet and Clark write: "Since it is clear that we do not know how to control serious influenza, the most important activity during a pandemic is to obtain knowledge whose analysis may lead to eventual methods of control." The English and American workers are using killed vaccines injected subcutaneously for immunization, and the authors employ egg-adapted attenuated living virus sprayed intranasally. Each has had a moderate degree of success in stimulating the production of antibodies in subjects whose earlier level was low, but little success in sub-

[1] "Monographs from the Walter and Eliza Hall Institute of Research in Pathology and Medicine, Melbourne; Number Four: Influenza, A Survey of the Last 50 Years in the Light of Modern Work on the Virus of Epidemic Influenza", by F. M. Burnet and Ellen Clark; 1942. Melbourne: Macmillan and Company Limited. Crown 4to, pp. 126, with 20 illustrations. Price: 17s. 6d. net.

jects whose previous level was high, and neither has been as effective as a natural attack of the disease. Two problems therefore arise in the face of a pandemic. Firstly, if present methods are to be extended, an enormous amount of killed vaccine will be needed for the subcutaneous method, and very careful maintenance of the attenuated living virus for the nasal spray; and secondly, if the pandemic virus proves to be antigenically remote from the known ones, much time will be required for testing the new strain, and in the Melbourne method especially, for producing the desired degree of attenuation, before mass production methods can be employed. Burnet and Clark's ambition for an ideal plan of investigation is tempered by a realization of the practical limitation of circumstance; it is to be hoped that other centres of research share their vision sufficiently to plan so that the greatest amount of information may be gathered by all. This is most necessary if in the future the scourge of pandemic influenza is added to what the authors aptly phrase "the human disorganisation called war".

The book is a worthy companion to "The Production of Antibodies" in the same series, but should be read by a much wider section of the profession. While it is to be regretted that the subject is one in which polysyllabic phraseology is indispensable, even in its own criticism, the clarity of thought and diction of the authors shines out, and that is perhaps their greatest gift to seekers after knowledge of this most difficult and fascinating of diseases.

GRAY'S ANATOMY.

IN their preface to the twenty-eighth edition of "Gray's Anatomy", the editors ask that they may be pardoned for asking for some degree of indulgence from its readers and reviewers owing to the unprecedented circumstances which have surrounded its preparation and production.[1] We feel that on the contrary, the editors and publishers should be warmly congratulated, for as we happen to know, the publishers must have overcome almost insuperable difficulties. Their main warehouses and stocks were burnt out three times in December, 1940, and May, 1941, and as everyone knows the editors both belonged to the heavily blitzed Guy's Hospital Medical School.

Turning to details, one may remark on the general improvements made by Mr. Maxwell and Miss la Riviere in the illustrations. This applies to the previous edition, but has been much extended in the new figures of the cranial and spinal nerves, of the muscles and some of the bones. In many cases the figures have been redrawn and greatly improved (for example, the striking figure by Mr. Maxwell of the dissection of the course of the facial nerve, Figure 957).

The inclusion of the new X-ray plates referred to in the preface is also of value.

In the text, special reference may be made to Dr. Denny-Brown's summary upon the functional significance of the cerebellum, a most valuable epitome of a difficult subject.

The revised section on the ductless glands, while much improved, is still defective, especially as regards illustrations of the microscopic structure of the spleen, the suprarenals, the thyreoid gland *et cetera*. More vigorous handling of this section and the inclusion of the hypophysis and pineal bodies (at present in the section on neurology) would be a further improvement.

In the section on muscles, much new detail has been incorporated concerning muscle action, and it may be remarked here that one value of recent editions is the constant reference by footnotes to any recent research work which may have altered or extended our knowledge. The illustrations of this section have been improved particularly by colouring.

In criticism, it may be suggested that a reasonably complete account of muscles and muscle action could nowadays include a tabulation of their action in various reflexes and a consideration of the antigravity muscles in the erect posture and in walking, while the account of the microscopic structure should include an account of the "motor unit" and of the "A1", "A2" and "B" sensory endings of muscle spindle and tendon; in the discussion of muscle action much of the earlier work of such pioneers as Beevor has yet to be incorporated. One of the weakest features of the book is the bone illustrations, though here the editors have possibly endeavoured to preserve what must have been one of the outstanding characters of the first edition. The improvement in modern standards is well shown by Miss la Riviere's Figure 268 of a typical thoracic vertebra, compared with Figure 316 of the base of the skull. This has an absolutely featureless squamous part of the occipital bone, though this is condoned by the excellent figures of the occipital bone by itself.

So one could continue with alternate praise and minor criticisms, but as a general impression we should like to end on a note of praise for the accuracy, breadth combined with detail, balance and all-round "up-to-dateness" of the "War Gray" and finally of pride in such an achievement by British anatomists and publishers in the war years 1940, 1941.

[1] "Gray's Anatomy Descriptive and Applied", edited by T. B. Johnston, M.D., and J. Willis, M.D., M.S.; Twenty-Eighth Edition: 1942. London: Longmans, Green and Company. 10" × 6¼", pp. 1576, with 1,347 illustrations, of which 631 are in colour. Price: 60s. net.

TUBERCULOSIS IN CHILDHOOD.

"TUBERCULOSIS IN CHILDHOOD", by Dorothy S. Price, is a small book which merits the attention of everyone interested in this branch of medicine and especially of those engaged in tuberculosis surveys of children.[1] Henry F. MacAuley has contributed a chapter on bone and joint lesions and other forms of extrapulmonary tuberculosis.

Following three chapters on classification, epidemiology and routes of entry of the bacillus, the author deals in turn with diagnosis, clinical manifestations and treatment. Right through the book emphasis is laid on the value of tuberculin tests and of radiology in diagnosis. The various skin tests are described. It is agreed that the intracutaneous tests are the most reliable, though in younger children preference is expressed for the Hamburger test followed when there is no reaction by the Mantoux test in which a dilution of 1 in 100 of old tuberculin is used. The value and the limitations of radiology in diagnosis are clearly stated. On page 33 the author remarks: "In certain cases radiological diagnosis alone is impossible, for example, between a primary tuberculous infiltration and an acute or unresolved pneumonia: so also are the interpretations of shadow in the hilar region etc."

The book is well illustrated and the case examples are well chosen. The author has a refreshing and sane outlook. This book is confidently recommended.

[1] "Tuberculosis in Childhood", by Dorothy Stopford Price, M.D. (Dublin), with a chapter on tuberculous orthopædic lesions and other contributions by Henry F. MacAuley, M.Ch., F.R.C.S.I.; 1942. Bristol: John Wright and Sons Limited. London: Simpkin Marshall Limited. 7¼" × 4¾", pp. 222, with 87 illustrations. Price: 17s. 6d. net.

Notes on Books, Current Journals and New Appliances.

MINOR PROBLEMS OF MEDICINE.

A BOOK containing 24 essays on minor problems of medicine has been published as one of "The Practitioner Handbooks".[2] Several volumes in this series have already been published, and some of them have been noted in these columns. Most of the contributions in the present volume have already appeared in *The Practitioner*, and when necessary the author has revised his matter and brought it up to date. The volume is edited by Sir Humphry Rolleston and Dr. Alan A. Moncrieff. The editors point out in the preface that an effort has been made to produce a manual of everyday medicine, which, although qualified by the word "minor", deals with maladies that play a major part in the discomfort of the individual and eventually in the health and well-being of the nation. For example, Sir Adolphe Abrahams writes on chronic constipation, Dr. T. L. Hardy writes on minor disturbances of digestion, Dr. John Craig discusses the treatment of stomatitis, Dr. F. E. Saxby Willis deals with acute sore throat, and Dr. Ivor J. Davies with influenza. Dr. R. W. B. Ellis writes on infantile convulsions, Dr. H. L. Parker on migraine, Dr. M. G. Good on rheumatic myalgias, and F. E. Hellier on corns, warts and boils. The book is likely to be useful to practitioners who look for advice on these ordinary subjects and have not a great deal of time to spare.

[2] "Minor Medicine", edited by Sir Humphry Rolleston, Bt., G.C.V.O., K.C.B., M.D., F.R.C.P., and Alan A. Moncrieff, M.D., F.R.C.P.; 1942. London: Eyre and Spottiswoode (Publishers) Limited. 8¾" × 5¾", pp. 223, with 14 illustrations. Price: 16s.

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MALIGNANT DISEASE OF THE PROSTATE.

DURING the last few years many additions have been made to the knowledge of malignant disease of the prostate. It used to be regarded as a rare disease, and though fortunately it cannot be looked upon as common, it is known to occur much oftener than was previously supposed. There was a time when degeneration of an hypertrophied prostatic lobe was said to be the chief cause of cancer of the prostate. Ewing in 1928 wrote that the chief condition predisposing to prostatic cancer was chronic hypertrophy. Nine years later, in 1937, H. H. Young stated that prostatic hypertrophy and prostatic cancer were distinct in their origin and that half of the cases of cancer of the prostate were associated with prostatic hypertrophy. Nowadays clinicians who wish to be accurate do not apply the term prostatectomy to an operation at which adenomata from the tissues surrounding the prostatic urethra are removed after suprapubic cystotomy. If they do use the word it is for the sake of convenience or from force of habit. With the growth of the adenoma in the lateral lobes the tissue of the prostate proper is compressed and is found chiefly in what is known as the posterior lobe. MacCallum in his text-book of pathology writes that Reischauer holds that the masses in the prostate begin as tumour-like growths of muscle and connective tissue in the mantle of the prostatic urethra and that any participation of glands in the formation of such a fibromyomatous nodule results from their contact and inclusion in its growth. If the mixture occurs early enough it produces a fibroadenoma, but Reischauer on the whole looks on the tumour as similar to a myoma in the uterus. Grassmann finds that the localized tumour arises from the peritubular framework of lateral urethral glands and similar accessory glands in the floor of the bladder and that the sprouting of these glands mixes with fibrous and muscular tissue to produce a fibromyoadenoma. The practical point is that when prostatic adenomata have been shelled out the tissue of the prostate proper remains behind and is still a potential focus for the growth of malignant disease. As a matter of fact it is not an uncommon experience in large urological clinics to see from time to time a patient in whom malignant disease of the prostate appears ten or twelve or more years after what is known as prostatectomy has been performed. It is thus clear that cancer may occur as a secondary change in a prostatic adenoma or as a primary manifestation in the prostate proper. Boyd, in referring to the abandonment of the idea that cancer occurs only as a malignant degeneration of an already hyperplastic gland, states that hyperplasia may be present as an associated condition in about 50% of cases of cancer. It would be difficult to determine the incidence of cancerous degeneration in prostatic adenoma. To begin with, prostatic hypertrophy is almost invariably present in some degree in men of advancing years, but few of these persons are submitted to operation and by no means all the specimens removed at operation are sent to a pathologist for examination. Young once stated that 20% of the patients who came to him with obstruction to urination had cancer of the prostate. He writes in his autobiography that Arnold Rich, of Johns Hopkins Hospital, recorded the observation that in 292 consecutive autopsies on men over forty years of age cancer had been found in the prostate gland in 41 cases, or 14%. Further R. A. Moore reported from Vienna that he discovered cancer of the prostate in 18% of 242 consecutive autopsies in men over forty years of age. This gives some idea of the incidence of prostatic cancer in general. In regard to primary prostatic cancer J. E. Kahler,[1] of the Mayo Clinic, reported in 1938 the results of a study of a large number of prostate glands yielding 195 cases of primary carcinoma. He found that carcinoma of the prostate occurred in 17·3% of men over fifty years of age. But only 53 of the 195 carcinomata were recognized macroscopically at autopsy. Only six of the carcinomata were squamous celled; all the others were adenocarcinomata. Of the carcinomata recognized clinically or grossly at autopsy 51% were accompanied by metastases in the lymphatic glands, lungs and pelvic peritoneum. Kahler found no relationship between prostatic carcinoma and associated atrophy, nodular hypertrophy, inflammation and calculi.

In regard to a cancer, associated with prostatic hypertrophy, developing within the hypertrophic tissue, the diagnosis and treatment in the early stages need not be considered apart from the diagnosis and treatment of simple hypertrophy. If the hypertrophied tissue is removed by enucleation of the affected areas, nothing remains to be done. Primary prostatic cancer most commonly originates in the posterior subcapsular stratum or lobe. It starts as a hard nodule which, being in the posterior lobe, may easily be palpated on rectal examination. If such a nodule is detected and a diagnosis is made, the problem of treatment is not simple. The only operation which will remove the growth is complete radical prostatectomy, of the type devised by Young. His perineal operation for the complete removal of the prostate is an heroic procedure. The urethra is divided as it leaves the prostate, the dissection is carried upwards and the bladder is opened. Eventually the whole of the prostate with its capsule, the prostatic urethra, the neck of the bladder,

[1] *Proceedings of the Mayo Clinic*, Volume XIII, 1938, page 589; abstracted in "Surveys and Abstracts", 1939, of "The British Encyclopædia of Practical Medicine".

the seminal vesicles and *vasa deferentia* are removed in one mass. Only the most expert surgeons are capable of undertaking such a procedure, and on this skill the patient's subsequent comfort, particularly in regard to vesical control, will depend. As far as can be gathered, this operation has not been extensively used in this country. Some surgeons hold that such an operation is seldom justified, partly because of its extensive nature, but chiefly on account of the necessary interference with the neck of the bladder and the great likelihood that the patient, if he recovers, will be left with permanent incontinence of urine. But even if surgeons are willing to undertake the task, the patient is seldom seen before the time for radical treatment has passed and only palliative treatment is possible.

During recent years progress has been made in the palliative treatment of prostatic cancer and some interesting papers dealing with the subject were read at a symposium before the Section on Urology at the annual session of the American Medical Association in June, 1942.[1] The papers that are published, six in number, are chiefly the outcome of the work that has been done on the prostate in recent years in the fields of endocrinology and biological chemistry. Work of this kind is not widely known among medical practitioners; the possibilities of treatment should be recognized, and even if such recognition does little more than emphasize the need for clear thinking in regard to prostatic diseases and also the advantage to the patient of early diagnosis, time devoted to a study of the subject will be well spent. Clarity will possibly best be served if the general conclusions are stated first. Anyone who studies the six papers in the symposium and the subsequent discussion will realize that the methods of treatment suitable for use in malignant lesions of the prostate that cannot be removed with comparative ease and safety, include transurethral resection to relieve obstructive urinary symptoms caused by the disease, together with irradiation therapy, orchidectomy and the administration of œstrogens, either alone or in various combinations. In addition the acid phosphatase content of the blood will be appreciated as an index of tumour or adult prostatic epithelium activity. Considering these subdivisions of the subject one by one, we note Thompson's statement that radical prostatectomy, the operation already discussed, has not been employed at the Mayo Clinic for the past ten years. Thompson discusses 887 cases of malignant disease in which transurethral resection was performed during the period 1924 to 1941. This group is composed of patients who had symptoms of urinary obstruction. In 95% of the cases the disease had spread beyond the confines of the gland when the patients first came under observation. From this two observations may be made. The first is that at the Mayo Clinic, which has no lack of skilled surgeons, the radical operation is not performed in the 5% of cases in which Thompson admits that the operation might be justified as a hopeful method of cure. There is thus a good precedent for the refusal of surgeons to undertake the procedure. The second observation has to do with the delay shown by patients in seeking advice for so dire a malady. Creevy sums up very well the reasons for the late discovery of the disease. In the first place prostatic carcinoma causes no symptoms until it interferes with urination or produces pain by local extension or metastasis. In the second place three-quarters of the cases arise in the posterior lamella at a relatively great distance from the urethra, and for this reason obstruction is a late manifestation. Thirdly the average carcinoma of the prostate grows slowly—Creevy quotes cases in which patients lived for eight, nine and thirteen years after evidence of the disease was forthcoming. Fourthly about 8% of prostatic cancers develop within spheroids of benign hypertrophy which hide them from the examining finger. In the fifth place most elderly men look upon a certain amount of urinary difficulty as inevitable in advancing years and delay in seeking medical advice until severe retention of urine or pain makes its appearance. Creevy's last reason is that many medical practitioners are not thoroughly aware of the serious significance of isolated hard nodules in the prostate. Returning to Thompson's views on transurethral resection we note his conviction that entirely adequate relief for long periods follows if the operation is properly performed. Not only is the patient given a normal bladder function, but there is practically no risk of the development of incontinence. Of the patients who survived operation, 23·5% were treated by irradiation. X-ray therapy was generally used, but in a few instances radon capsules were implanted in the prostatic capsule. In regard to survival rates reference may be made to a group of 337 who were operated on prior to 1937. Of the 334 who left hospital, 326 were traced, and of these 14·1% had lived for five years or more. In regard to treatment by irradiation therapy, Thompson is the only one of the authors who discusses it. In the subsequent discussion, however, A. D. Munger stated that improvement resulted in 85% of cases and that this improvement ran parallel to that occasioned by other types of castration. He thought it was more effective than the use of an œstrogen alone.

The results of orchidectomy are described by Alyea and Henderson and by Nesbit and Cummings. The former pair of authors publish a chart which shows the relationship between adult prostatic epithelium and hormones. Androgen activates the adult prostatic epithelium and increases the acid phosphatase content of the serum. Castration removes androgen and œstrogen neutralizes it; as a result in each case the prostatic epithelium is inactivated and the acid phosphatase content of the serum becomes less. Alyea and Henderson state that the most striking feature after orchidectomy is the rapid relief of pain due to metastases. They performed orchidectomy on fourteen patients who had no evidence of metastasis. When they wrote their article orchidectomy in one instance had been performed twelve months before. Alyea and Henderson liken this form of treatment to sterilization undertaken for malignant disease of the breast. Nesbit and Cummings report that 48 of 75 patients received considerable benefit from orchidectomy—repression of the neoplasm occurred, the patients increased in weight and all who had pain became free of it. In spite of the failures in their series these authors regard the procedure as worth-

[1] E. P. Alyea and A. F. Henderson: "Carcinoma of the Prostate: Immediate Response to Bilateral Orchidectomy", *The Journal of the American Medical Association*, December 5, 1942, page 1099; C. D. Creevy: "Diagnosis and Treatment of Early Carcinoma of the Prostate", *ibidem*, page 1102; G. J. Thompson: "Transurethral Resection of Malignant Lesions of the Prostate Gland", *ibidem*, page 1105; R. M. Nesbit and R. H. Cummings: "Prostatic Carcinoma Treated by Orchidectomy", *ibidem*, page 1109; A. B. Gutman: "Present Status of Serum 'Acid' Phosphatase in Patients with Carcinoma of Prostate", *ibidem*, page 1112; W. P. Herbst: "Biochemical Therapeusis in Carcinoma of Prostate", *ibidem*, page 1116.

while. In both these reports on orchidectomy the period of observation has not been long enough for any real estimate of the value of orchidectomy to be made. The procedure is admittedly only palliative, but in spite of this the relief from pain, even if it should prove to be only temporary, may well justify its performance. The effect of the administration of œstrogens is, as already pointed out, much the same as that of orchidectomy. Herbst points out that the object of œstrogen administration is the maintenance of a low androgen and acid phosphatase level in the blood. He has succeeded in doing this for a period of twenty-two months. Herbst states that research is necessary to determine the extent to which control can be obtained by biochemical means. That there is a useful sphere for such treatment seems clear, even if the clinician goes no further than to seek the relief of his patient's pain. The significance of a rise in the acid phosphatase content of the serum is well explained by the statement of Alyea and Henderson: " . . . acid phosphatase is found in largest amounts in the adult prostatic epithelium and carcinoma of the prostate which is a tumor composed of this cell. When metastasis takes place, the tumor cells are expressed into the blood stream and lymphatics and cause a rise in the serum acid phosphatase. Therefore this is an indication of tumor or adult prostatic epithelium activity."

From the short account that has been given of the work covered by the American symposium, it will be clear that the illness of the sufferer from prostatic carcinoma may be made more bearable than it used to be and that life may possibly be prolonged without undue suffering. There is no doubt that further progress will be made in this important subject.

Current Comment.

THE PREVENTION OF COLDS.

Millions of dollars' worth of vitamin preparations are sold each year in the United States, and it is said that much of this buying is stimulated by advertising which suggests that vitamins will prevent colds. A similar statement might be made about our own community. It has, of course, been shown by repeated experiments that both animals and man have a decreased resistance to infections of various kinds when suffering from vitamin deficiencies, so that if the diet of an individual who is always "catching cold" is deficient, it is sound common sense to make up the deficiency. But it has certainly not yet been shown that the addition of any of the vitamins to a reasonably adequate diet produces increased resistance to infections of the upper respiratory tract. Donald W. Cowan, Harold S. Diehl and A. B. Baker[1] have investigated the value of large doses of vitamin *C* alone, and also of large doses of mixed vitamins in the prevention of colds. In this as well as in their previous studies, the subjects were all students of the University of Minnesota who volunteered to take part in the experiments, because they were particularly susceptible to colds. Students applied for admission to the "Cold Prevention Group" after term commenced in the fall quarter. Those whose "colds" seemed to be due to chronic sinusitis or allergic rhinitis were excluded. Of the 427 students who enrolled, 183 were supplied with a quantity of 100 milligramme tablets of synthetic ascorbic acid and were instructed to take two such tablets daily throughout the "cold season", a total of twenty-eight weeks. Fifty other students were instructed to take two tablets daily for the first two weeks, then one tablet daily throughout the season unless and until an infection of the upper respiratory tract developed, in which case they were to take five tablets on each of the first two days of the cold. To serve as a control group, 194 students were supplied with placebo tablets of the same size, shape, appearance and taste. These students, of course, did not know that they were serving as controls. In the following year, 347 students were enrolled in a similar study, when multiple vitamins were used. As before, approximately half of the students served as controls. These studies gave no indication that either large doses of vitamin *C* alone or large doses of vitamins *A*, B_1, B_2, *C* and *D* and nicotinic acid had any important effect on the severity of infections of the upper respiratory tract when administered to young adults who presumably were already on a reasonably adequate diet. In the discussion that followed the reading of this paper, Dr. Harold S. Diehl, one of the authors, explained that the study was made as a challenge to the belief, stimulated by advertisements, that large doses of expensive vitamins would prevent colds. The important part of the study was the presence of a control group, members of which were given something that had the same psychological effect as the treatment received by the group on which experiments were made Placebos frequently gave what appeared to be excellent results. In fact, certain results reported by many persons who received placebos would serve as splendid testimonials for any medicament devised to prevent colds.

The work of Diehl and his associates is of interest, but a study such as this cannot claim to belong to the class of accurate dietary experiments. It is, however, a warning to those who pay too much attention to commercial advertising.

Adequate and well-balanced diets are important, but do not necessarily build up resistance to any particular infection. Resistance to infection seems to be a specific quality: specific, that is, to the causal organism concerned. It can probably be acquired only by specific immunological procedures or by experience of the infection itself.

[1] *The Journal of the American Medical Association*, December 19, 1942.

SCABIES, THE ARMY AND INTELLIGENCE.

Writing in the *British Medical Journal* of March 1, 1941, G. A. Hodgson, an officer in the Royal Army Medical Corps, reported the result of an investigation in which he examined one hundred unselected scabies patients and a control group of five hundred consecutive recruits. He subjected these men to intelligence tests and reported that scores suggesting subnormal and low-grade intelligence were found "in great excess" among the scabetic patients. This finding would be quite understandable were it the result of an investigation in ordinary civil life, but conditions of life in the field on active service would suggest that further investigations should be made along the same lines. Attention is therefore drawn to a communication by Kenneth Mellanby, A. L. Northedge and C. G. Johnson.[1] The investigations of these authors covered a series of 250 scabetic men and it was found that they approximated mentally the standard of an ordinary sample from the army; at the same time there were perhaps among the patients a rather low proportion of men with superior intelligence. It was thought that possibly the men with "larger parasite populations" might be men of lesser intelligence, but the men who harboured a larger number of parasites gave a slightly higher score in the tests than those whose parasites were not so numerous. Further, no significant difference in intelligence was discovered between men who reported sick and those whose infestations were discovered on routine examination. Mellanby, Northedge and Johnson suggest that Hodgson in his investigation used normal values that were too high because he took them from a selected population; had he not done this, they think that his results would not have been very different from their

[1] *The Lancet*, November 21, 1942.

Abstracts from Medical Literature.

BACTERIOLOGY AND IMMUNOLOGY.

Immunization of Fowls Against Plasmodium Gallinaceum.

PAUL F. RUSSELL AND B. N. MOHAN (*The Journal of Experimental Medicine*, November, 1942) have attempted the immunization of fowls against mosquito-borne *Plasmodium gallinaceum* by injections of serum and of inactivated sporozoites. This is an extension of previous work, in which only the inactivated homologous sporozoites were used. The same technique as in previous experiments was followed, the infectivity of the mosquitoes being proved by dissection. In the first series in which fowls had been treated with five doses of sporozoite vaccine intravenously, an agglutinating titre of 1 in 65,636 was produced, seven out of ten birds made a spontaneous recovery, and the highest percentage of red cells infected was 20·5. In the control series, four out of six died and the red cells showed 42·8% infection. When serum was used controls were given normal sheep serum and test birds pooled serum from fowls having chronic malaria due to the same plasmodium. The mortality in controls was 100%, while six of eight test birds made spontaneous recoveries. Finally some were immunized with sporozoites and given sheep serum, others were given sporozoites and protective serum; here the controls showed a mortality of 100% and the test birds nil, while the infection of the red cells of the controls was 41·7% and of the test birds 9·0%. The "normal mortality" of birds infected with *Plasmodium gallinaceum* is 55·4%. The authors succeeded in reducing it by each method, but most markedly by a combination of the two. The prepatent period was not altered.

Diphtheria Immunization.

JOHN J. PHAIR (*The American Journal of Hygiene*, November, 1942) discusses the interpretation of the Schick test. The development of delicate methods for the estimation of blood antitoxin in samples taken at the same time as the test was performed, had provided evidence that the threshold between positive and negative responses in skin reactions was about 0·01 unit per cubic centimetre, although some reactors had shown they could produce appreciable amounts of antitoxin in response to very small stimuli. In every series of the author's tests there was a small percentage of "negative" reactors in whom no demonstrable antitoxin could be found, but the general agreement between antitoxin level and Schick readings was very high. A series in which the subjects had received toxoid by intranasal administration one month before showed much more complete agreement, and it was thought that the previous "antigenic history" of the subject might be of great importance. The author suggests that some defence mechanism other than the production of antitoxin determines whether or not a strain of *Corynebacterium diphtheriæ* is successful in its invasion attempt. In infants a positive response to the Schick test indicates susceptibility; in adults it merely indicates deficient circulating antitoxin, or an inefficient antibody mechanism, not necessarily susceptibility to clinical attack; but while the antitoxin level is determined by a single observation, the skin reaction shows the response to a given stimulus, and this is of the greater importance.

Antimalarial Effect of Acranil in Birds.

WENDELL D. GINGRICH AND ROLLIN S. FILLIMORE (*The American Journal of Hygiene*, November, 1942) have tested the antimalarial effect of acranil in birds. The drug, which is one of the acranil series, was found to be toxic to canaries in aqueous solution, and was therefore administered in 5% gelatin. A control series of 30 canaries was infected with *Plasmodium cancetherium*, and developed acute symptoms in two to five days, and then the test series was infected and treated prophylactically for five days. The incubation period before the appearance of parasites in the blood was lengthened, and the duration of the illness shortened. Two series were treated with "Atebrin" and acranil during the acute rise of the infection. Blood smears became normal in two to four days with acranil, and in two to five days with "Atebrin". The segmentation rate was slightly diminished and there seemed to be less persistence of gametocytes. The authors believe the drug investigated has a plasmocidal effect comparable to but shorter than that of "Atebrin", and is effective because it protects the host from the severe attack until the immune response is adequate.

Formation of Antibodies.

W. E. EZRICH AND T. N. HARRIS (*The Journal of Experimental Medicine*, October, 1942) have studied the formation of antibodies in the popliteal lymph node of the rabbit. Cell production was observed at the same time, also structural changes in the glands, which were excised from rabbits inoculated on the same day, but sacrificed on different days. Antigens used were typhoid bacilli and sheep red cells, and the antibodies tested for were agglutinins and hæmolysins. A technique was evolved for the collection of afferent and efferent lymph, in quantity sufficient for the tests named. In the areas of injection the afferent lymph titres remained low during the nine days of the experiments, while in the efferent lymph from the single gland great increases in titre took place, later increases occurred in the cell count of the lymph, and the gland itself increased in size up to almost five times its original weight. The responses to injection of typhoid bacilli were in general more marked than the responses to sheep red cells. In the earlier stages a few granular leucocytes and some monocytes were present in the efferent lymph, but these disappeared, and when the agglutinin titre rose sharply on the sixth day, the lymphocyte count was at its highest and the germinal centres were most active, and small foci of epithelioid cells were noted in the typhoid experiments. The authors believe that antibodies are not the product of the reticulo-endothelial system alone, and the fact that the tissue response is so markedly lymphocytic, points to the fact that lymphocytes should be considered as a factor in antibody production.

Death in Malaria.

R. H. RIGDON (*The American Journal of Hygiene*, November, 1942) has offered a consideration of the mechanism of death in acute malarial infection, with a report of a case. The patient was a white female child whose illness lasted only nine days, malaria being diagnosed on the day of death, and only one dose of quinine was given intravenously. At autopsy spleen and liver were grossly swollen, the heart was pallid, there were hæmorrhages beneath the diaphragm and the intestinal mucosa. Pigment was present in sections of brain capillaries where parasites were most abundant, there were hæmorrhages, and phagocytosis was prominent in the lesions. Smears taken from the peripheral blood four hours before death showed that 15% of red cells contained parasites, and the heart blood was not clotted at the post-mortem examination. The author thinks that progressive anæmia, producing comparatively sudden anoxæmia, altered the permeability of the capillaries, and that the plugging of these small vessels with tightly packed red cells was comparable with the phenomenon of experimental shock. This phenomenon has also been noted in experimental infection of monkeys with *Plasmodium knowlesi*, where the appearances have been photographed in the circulation. This patient presents evidence to support the author's explanation for the mechanism of death.

Plasmodium Lophuræ in Young Ducks.

R. I. HEWITT, A. P. RICHARDSON AND L. D. SEAGER (*The American Journal of Hygiene*, November, 1942) have continued their studies by making observations on untreated infections with *Plasmodium lophuræ* in 1,200 young white Pekin ducks, one to twelve weeks old, raised from one day in the laboratory. The ducks were inoculated intravenously with varying numbers of parasites, and when infection appeared, daily counts of parasites per 500 red cells and estimations of hæmoglobin were made. With larger inocula, the latent period before appearance of parasites was shorter, and the percentage of deaths higher and more quickly produced. If a dose of one to ten billion parasites per kilogram was used, the latent period was regularly six to seven days, and 90% of birds died within twenty-five hours. This stability of results was maintained when a large group of birds was tested and recorded as a suitable technique when the work later extended to the testing of possible chemotherapeutic agents. The hæmoglobin dropped sharply within twenty-four hours of the peak value of the parasite count, and was so constant that the occurrence of the peak was certain even if the count was not known. If birds of different ages were given similar inocula, their early reactions were similar, but a higher percentage of deaths occurred in the older birds. Some evidence was obtained of differing virulence in two strains of parasite used, but providing parasite dose and age of bird were controlled, comparable

results could be obtained. The authors believe that they have evolved a technique by which they will be able to test both qualitatively and quantitatively drugs whose plasmocidal effects are under investigation.

Entamœbæ in the Stools of Rhesus Monkeys.

DAVID RICHARD LINCOMBE (*The American Journal of Hygiene*, November, 1942) has studied the fluctuation of cysts of *Entamœba histolytica* and *Entamœba coli* in the stools of rhesus monkeys. The animals were maintained on a diet of strained bananas, the cyst content was examined on alternate days by a uniform technique in duplicate portions, and the number of cysts eliminated for a twenty-four-hour period was calculated. Graphs were constructed from the figures and suggested that there was a cycle of six to seven days from peak to peak in the number of cysts, the peak being followed by a rapid fall within forty-eight hours. *Entamœba coli* consistently gave higher figures than *Entamœba histolytica*. These numbers were absolute, and had no relation to the water content of the stool, or to the total weight passed. One animal was then kept as a control, while the other was given an addition of protein to its diet, and the level of cyst production fell considerably. Seasonal factors were eliminated by repeating the tests at an interval of four to five months. The authors suggest that a negative diagnosis for entamœbæ should not be made unless several examinations spread over eight to ten days have failed to show the presence of cysts.

Bactericidal Substances from Fungi.

W. H. WILKINS AND C. C. M. HARRIS (*The British Journal of Experimental Pathology*, August, 1942) have made a preliminary report on an investigation into the production of bacteriostatic substances by fungi. One hundred species were tested for substances active against *Staphylococcus aureus*, *Bacterium coli* and *Pseudomonas pyocyanea*. Nine penicillia, eighteen aspergilli and three *fungi imperfecti* gave results which the authors felt would justify further investigation.

HYGIENE.

The Immunization Programme in the Royal Canadian Air Force.

A. H. SELLERS (*Canadian Public Health Journal*, December, 1942) states that the immunization programme of the Royal Canadian Air Force includes vaccination against smallpox, combined "T.A.B." vaccination, vaccination with tetanus toxoid (three doses of one cubic centimetre at intervals of three weeks and yearly reinoculation), the use of the Schick test and Dick test, the use of scarlet fever toxin (five doses at weekly intervals to all who react to the Schick test). Altogether this takes six weeks. A sterile syringe containing epinephrine is kept ready for use in the occurrence of immediate severe reactions. Personnel are kept under observation for half an hour afterwards, and 1% of males and 2% of females require "excused duty". A reduction of 90% can be obtained in diphtheria. To scarlet fever 70% of men were immune and 54% of women. About 20% had never been vaccinated. No tetanus and only three cases of typhoid fever have been met with in the past two and a half years, while of diphtheria, since immunization was brought in, only nine cases have occurred. About 0·6% develop scarlet fever, a much lower figure than in civilian life.

The Modern Public Opinion Poll.

P. D. GUERNSEY (*American Journal of Public Health*, September, 1942) writes that in the public opinion poll hundreds of ordinary citizens are seen by trained interviewers, questioned and given a ballot form to fill in. The name is not required, but information is sought—age, sex, nationality, economic status and suburb are added to their opinions—and interviews are apportioned equally to these controls. Representatives of a typical cross section are looked for, not the mass bulk of the "straw votes". Thus a picture of public opinion on a given problem at a given time is obtained. A trained staff is needed. These public opinion studies are found of real value for directing popular education and providing a basis for future planning. The ballot at Rochester dealt with the care of the sick and about fifty questions were asked. About 5% sought aid from osteopaths *et cetera*, but only 5% picked their doctor on his record; 92% favoured hospital insurance; 80% thought a family could pay $1.30 a month for this; 72% favoured extension of the scheme to medical and surgical care. Only 22% thought $3 a month should be paid for this extension and only 15% said that they could not get medical care because of its cost. Among this 15% the conditions noted were all chronic disorders. Over a third of the poor did not know how to go about getting free medical care at home.

The Incidence of Trichomonas Vaginalis.

E. KUITUKNEN-EKBAUM AND EVA MADER MACDONALD (*Canadian Public Health Journal*, December, 1942) describe the incidence of *Trichomonas vaginalis* in clinic patients at the Women's College Hospital, Toronto. Among 300 women patients aged fourteen to sixty-five years the organism was found in 112 or 37%. In 101 cases discharge was found, but in 117 discharge was present without trichomonas. None of the organisms was met with in women over the age of forty-eight years.

Ætiology of Acute Illness among Workers using Low-Grade Stained Cotton.

ROY SCHNEITER, PAUL A. NEAL AND BARBARA H. CAMINITA (*American Journal of Public Health*, December, 1942) discuss an acute illness which occurs among workers using low-grade stained cotton. Within six hours after exposure acute fever lasting forty-eight hours was ushered in by conjunctival irritation, dry throat, cough, aches and pains all over, resembling an intoxication. No insecticides or toxic gases and few fungi were found in the stained cotton, but Gram-negative rods in great numbers, probably an aerobacter. A heat-stable, endotoxin-like substance was found in filtrates of extracts from the cotton and in killed suspensions of the organism; intradermal injections of this substance brought about inflammatory conditions typical of an intoxication.

Effect of Aluminum Hydroxide Sedimentation, Sand Filtration and Chlorination on the Virus of Poliomyelitis.

J. EMERSON KEMPF, MARTHA G. WILSON, MARJORIE E. PIERCE AND MALCOLM H. SOULE (*American Journal of Public Health*, December, 1942), using two distinct strains of poliomyelitis virus from monkey cord, found that virus was not removed from water by alum sedimentation and filtration methods which removed 99·6% of *Escherichia coli*. An alum sediment of 1·50 millilitres per litre did remove the virus from water, the sediment remaining infective. This was a higher concentration than in several water plants tested. To inactivate the more resistant strain 1·5 parts per million for 25 minutes was needed. One part per million was needed by the less virulent strain. These chlorine concentrations are in excess of those used in ordinary water supplies and swimming baths.

Effect of Hibernation on Content of Coliform Bacteria in Oysters.

JAMES GIBBARD *et alii* (*American Journal of Public Health*, September, 1942) state that in the Canadian Atlantic oyster beds the water temperature is below 0° C. for months. Feeding activity begins at 5° C. Potentially dangerous oyster beds exist close to Buctouche village. The sewage flows into the river; the impervious soil favours stormwater contamination and increases pollution. When freezing cuts out surface drainage the coliform content reaches a low level and the coliform content of the water varies with that of the oysters. Below 0° C. coliform organisms are absent. Gross pollution may make the use of oysters unsafe at any time, but many areas dangerously polluted in warmer weather are safe when covered with ice. Two weeks after the final formation of ice appears the safe limit.

Thiamin Content of Milk in Relation to Vitamin B_1 Requirement of Infants.

ELIZABETH M. KNOTT (*American Journal of Public Health*, September, 1942) has investigated the thiamin content of milk in relation to the vitamin B_1 requirement of infants. Growth assays were found most reliable. Pasteurized milk gave 26 microgrammes per 100 millilitres of milk of 6·8 pH; if boiled three minutes the figure was 24. Evaporated milk gave values of 13, 19 and 27. Breast milk of 17 women yielded three to eighteen microgrammes, with an average of 9 at a pH of 8·1. Diet of the mother is most important. A study of excretion in urine when the infant receives stated amounts indicated that 80 microgrammes meet the baby's needs. If blood cocarboxylase content rises to about 5 microgrammes per 100 millilitres, well-being seems assured; a figure of 3 to 4 seems enough ordinarily, but in times of stress the extra thiamin is advised.

Medical Societies.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held at the Institute of Medical and Veterinary Science, Adelaide, on May 1, 1942.

The Distribution of Diseases in the Southern Pacific.

CAPTAIN C. M. DELAND presented a paper on "The Distribution of Diseases in the Southern Pacific". He said that to understand the subject it was needful to realize (i) the geological history of the area, (ii) the racial migrations which had populated the area, (iii) the diseases introduced by the white man's transport.

In regard to the geological history, Captain Deland said that the Australian region included Australia, New Guinea, and all the East Indies and Pacific islands east of Wallace's Line, that narrow water division which was one of the oldest dividing lines on the earth's surface. Animals and plants which were immigrants had to pass this line from Asia and then spread as their invasion transport allowed, from Asia to the east; this explained the distribution of the vectors of disease. The islands beyond New Guinea and Australia were of volcanic and coral origin, and had never formed part of a continental mass, at least in reasonably late times. Thus all inhabitants were invaders and colonizers who reached their present homes by air or sea transport of some kind. As one travelled east from Asia, the further one went, the fewer the invaders. The presence of snakes ended at the Solomon Islands, that of frogs at Fiji. The most outstanding point of medical interest in this fact was the distribution of the vector of malaria. In Asia, Australia, and parts of the mainland of New Guinea, there were a number of distinct species of *Anopheles* that carried malaria. Most of them were confined by fastidiousness in breeding places and by weakness of flight. But *Anopheles punctulatus* var. *moluccensis* was spread over a large area of New Guinea, the Solomons, the Santa Cruz group, the new Hebrides and the northern part of New Caledonia, and it carried malaria there. It bred in clean ground water exposed to the sun, so that anywhere would do. It flew well, so that it could be carried thirty miles or so down wind; but its larvæ would not carry in water bottles, coconut shells *et cetera*. It had therefore colonized the foregoing groups of islands, but its range, and thus that of malaria, was stopped by the long sea distances—roughly at the line of meridian 175°. Fiji, Samoa, Tonga, Tahiti and the French possessions in the south-east Pacific were free from that mosquito and therefore of malaria; so also were certain outlying islands further west, such as the Mortlock group.

Captain Deland then referred to racial migrations. He said that they had been important in the spread of disease, and like those of animals, they depended on the means of transport. The aboriginal inhabitants had been so long in place that they had lost what knowledge they must have had of navigation. After them came the Papuans, who had canoes sufficient for crossing rivers and for travelling short distances over smooth seas. They drove their predecessors inland and spread as far as they could, to New Guinea, to the nearer Solomon Islands, and down the east coast of Australia, taking with them malaria and frambœsia. They were followed by the Melanesians, better fighters, who drove them inland in their turn. But the Melanesians had canoes capable of undertaking rough sea crossings from land to land, which were the limit of their navigational knowledge. They spread as far as Fiji and New Caledonia and carried malaria with them. The navigational range of their canoes coincided curiously with the wind-borne range of *Anopheles*. Then came the Polynesian—no great fighter, perhaps, but the world's greatest primitive navigator. He could not drive out the Melanesian, so he navigated the thousands of miles to the farthest ends of the Pacific and colonized all but one or two isolated islands, which he missed only because of adverse currents. He took his diseases with him; but he outranged the vectors of malaria early. Perhaps he took the vectors of filariasis with him in his water vessels; but he outranged even those when he reached his farthest goals—New Zealand and the Gambier and low islands. In some of his outposts his diseases died out and a disease-free community was left. Such were the islands that carried a saturated population; they were tiny specks of land with attached reef, completely clothed with houses and coconut palms, whose populations lived entirely on sea food and coconuts, which formed a balanced diet.

Captain Deland went on to speak of the coming of civilization. First Malay and then European people arrived; they travelled in communities on ships and carried their sick with them. The Malay did not cover the whole Pacific, but he probably carried epidemics of smallpox and cholera. Perhaps he took ulcerating granuloma to its present homes in parts of New Guinea and Santa Cruz; perhaps he planted *Paragonimus* in New Ireland and leprosy in New Hanover. Then came the white man. He took with him his diseases, many of them to populations who had not known them for countless generations and had no natural resistance. Only syphilis and diphtheria failed to assert themselves—sypnilis because of the universal presence of frambœsia which conferred immunity to it, and diphtheria because for some reason it did not spread in the tropics. But above all, there were introduced epidemic infections, diseases that spread from man to man, and it was those that so greatly depleted populations and even (as in the case of the Anchorite group) totally destroyed them. The greatest of the killers was smallpox, which wiped out populations in many parts of the Pacific, such as those of Easter Island, the Marquesas *et cetera*. The epidemics occurred over a period of centuries; but smallpox had never remained endemic in any island. Outbreaks had occurred in recent times, such as that along the north of New Guinea just before the last war. The only other place where Captain Deland could recall seeing pock-marked natives was the island of Pentecost, in the New Hebrides. Other diseases that had caused severe or fatal epidemics were measles, influenza and bacillary dysentery. It was doubtful whether measles was the true cause of the enormous number of deaths in Fiji in the "eighties"; analysis of the records made it most probable that bacillary dysentery followed the measles and killed the victims. Captain Deland pointed out that the latter disease had remained endemic in many places and flared up occasionally to give rise to the most destructive epidemics known at the present time in the islands. Some of the minor infectious diseases caused epidemics when introduced, and because of the natives' tendency to "cool off" in cool water when feverish, they might be followed by complications. Rubella and whooping cough had become endemic in many islands. A peculiar form of pneumococcal bronchopneumonia caused fatal epidemics in New Guinea; it spread in a similar fashion to cerebro-spinal meningitis, under conditions of bad ventilation and crowding.

Captain Deland then said that with regard to epidemics he did not agree with the attitude taken by the quarantine authorities to the smallpox danger. In the Netherlands East Indies and around the main ports in New Guinea a considerable amount of vaccination had been carried out; but there was still an enormous non-immune population. All the islanders were good seamen in small craft, and they hated and feared the Japanese. Many might escape in *prahu* or canoes to the north of Australia and not to the ports of entry. Moreover, an unscrupulous enemy with a vaccinated army might be tempted to use smallpox as a weapon. He could easily introduce Chinese or natives with the disease.

Referring once more to the South Seas, Captain Deland said that tuberculosis was undoubtedly introduced by the European all over the Pacific, and it found a non-resistant population. It probably formed the greatest menace of all to the future of the native, and there was a great deal to be said in favour of a drastic policy of segregation. Leprosy was widespread in its endemicity, though only in a few places was it common. In New Guinea, New Hanover was heavily infected and a great deal had been done by segregation and modern treatment; the same was true of Fiji. But the word "leprosy" had a political sensation value and tradition, which had dragged the disease into notice to the exclusion of more important matters, such as tuberculosis. The island of Nauru had provided two unusual epidemics. It contained an isolated population, which for many generations had had no outside contacts at all. Chinese labour introduced leprosy, which promptly caused an acute epidemic in the totally non-resistant people. Then it was decided by moralists that the drinking of the fermented sap of the coconut was wrong, and this was prohibited; the result was an acute epidemic of infantile beriberi. Severe destruction of a non-immune population was caused when Buka labour carrying malaria was taken to Matty and Aua in New Guinea, where the *Anopheles* was present, but where there had been no malaria. The whole history of disease in the islands was bound up with the introduction of new disease into a non-immune population, and almost every known infection had been guilty at some time. Modern transport, and especially uncontrolled war transport, might repeat the crime again, and the population of Australia might be like

that of Polynesia if it did not "watch out". Captain Deland cited as examples yellow fever, the Asiatic flukes and cholera. He said that space would not permit him to refer to tropical ulcer or typhus, but he recommended those interested to read C. E. Gunther's discussions on typhus in THE MEDICAL JOURNAL OF AUSTRALIA.

Finally, Captain Deland said that there were a few diseases of civilization and cooler climates that did not exist in the islands. For some reason diphtheria did not spread, and virulent streptococci were practically absent. Tonsillitis, rheumatism, erysipelas and scarlet fever were not seen. That point had some practical importance in Australia. Children brought up in the islands had not been exposed and immunized to such streptococci; when they came to Australia they might suffer much from infections. Popular fancy put this down to tropical weakness and such nonsense. Those children were often greatly helped by injections of autogenous streptococcal vaccines.

Medical Practice.

APPROVED NAMES FOR DRUGS.

THE following document recently issued by the General Medical Council of Great Britain and sent to Dr. J. H. L. Cumpston, Director-General of Health, Commonwealth Department of Health, by the British Pharmacopœia Commission, is published for the information of medical practitioners.

During the war the General Medical Council has published, from time to time, on the recommendation of the British Pharmacopœia Commission, lists of approved names for substances produced by British manufacturers, in some instances under licence granted by the Comptroller-General of Patents, Designs and Trade Marks.

The intention has been to recognize non-proprietary names which could be used freely by manufacturers, and thus to provide a means of avoiding the difficulties to medical men and pharmacists which result from the use of a multiplicity of names for the same substance.

When any of the substances for which names have been approved have been admitted to the Pharmacopœia, the approved name has been made the official title, but the recognition of an approved name does not imply that the substance will necessarily be admitted to the Pharmacopœia.

The Pharmacopœia Commission have now formed an advisory Committee on Nomenclature to assist them in the selection of approved names.

Suggestions for suitable names will be invited from the manufacturers interested in the production of a substance for which an approved name is required, and full consideration will be given to the suggestions received.

The Commission hope that the approved names will be generally adopted, and would deprecate especially the introduction of new names for substances for which approved names have been published.

The Commission have adopted the following statement of principles as a guide in the selection of approved names:

1. Names should, preferably, be free from any anatomical, physiological, pathological, or therapeutic suggestion. This applies only to chemicals. Such suggestion cannot always be excluded in the naming of biological products.

2. The accurate chemical name should be used if suitable; when it is unsuitable the attempt should first be made to form a name by the combination of significant syllables from the scientific chemical name, and to include an indication of the potent element or constituent of a compound.

3. Names should be, in general, preferably of two, three, or at most four syllables.

4. Names should be distinctive in sound and spelling, and should not be liable to confusion with names already in use.

5. Names which are difficult to pronounce or to remember should be avoided.

6. The addition of a terminal capital letter or number should be avoided.

7. Names used in the current United States Pharmacopœia, or adopted for the next revision, should be used either as principal titles or as synonyms.

8. Names used in the British Pharmaceutical Codex or in New and Non-Official Remedies should receive preferential consideration.

9. The following terminations, which are now well recognized, should be used as far as possible: -ine (Latin—ina) for alkaloids and organic bases; -in (Latin—inum) for glycosides and neutral principles; -ol for alcohols and phenols (–OH group); -al for aldehydes; -one for ketones and other substances containing the CO group; -barbitone or -itone for drugs of the barbiturate group; -caine or -aine for local anæsthetics.

Approved Names Already Published.

Certain names originally published as approved names have now been made official by the inclusion of monographs in Addenda to the British Pharmacopœia, 1932.

OFFICIAL NAMES.	OTHER NAMES.
Third Addendum.	
Bromethol.	Avertin.
Carbachol.	Doryl.
Hexobarbitone.	Evipan.
Idoxyl.	Uroselectan-B.
Leptazol.	Cardiazol.
Mepacrine hydrochloride.	Atebrin.
Mepacrine methanesulphonate.	Atebrin musonate.
Nikethamide.	Coramine.
Phemitone.	Prominal.
Soluble Hexobarbitone.	Evipan Sodium.
Stibophon.	Fouadin.
Fourth Addendum.	
Pamaquin.	Plasmoquin.
Suramin.	Germanin (Bayer 205).

New official names were given to certain substances included in the British Pharmacopœia, 1932, and the Addendum, 1936. For those names reference should be made to the relevant publications.

APPROVED NAMES.	OTHER NAMES.
Amethocaine Hydrochloride.	Decicaine.
Cyclobarbitone.	Phanodorm.
Dienœstrol.	Di-p-hydroxyphenylhexadiene.
Diodone.	Perabrodil.
Diphenan.	Butolan.
Dithranol.	Cignolin.
Ethisterone.	Ethinyltestosterone; Lutocyclin; Lutogyl; Pregneninolone; Progestoral; Prolution C.
Hexazole.	Azoman; Triazole.
Menapthone.	2 - methyl - 1 : 4 - naphthaquinone (Menadione U.S.P. XII).
Meprochol.	Esmodil.
Mesulphen.	Mitigal.
Pethidine Hydrochloride.	Dolantin.
Pheniodol.	Biliselectan.
Pholedrine.	Veritol.
Soluble Phenytoin.	Epanutin; Eptoin Sodium Diphenylhydantoinate; Solantoin; Soluble Dilantin.
Sulphacetamide.	Albucid.

Correspondence.

THE REMOVAL OF PLASTER CASTS.

SIR: In reference to the article in THE MEDICAL JOURNAL OF AUSTRALIA of February 27, 1943, at page 189, you mention the method described by A. T. Andreason for the removal of plaster of Paris casts by the use of rubber tubing.

I should like to point out that, having had experience of this so-called "simple method", the following disadvantages were met with:

1. The scarcity of rubber, which was very much in evidence in Great Britain, especially during the last few months.

2. The liability of the tubing to snap (especially if old rubber is used)—thus, the lengths become shorter and shorter and useless.

3. The most important point: on removal of the tubing there is left the tunnel or so-called "dead space" in the plaster cast. If there is any œdema, and, of course, this occurs very frequently in both fresh plasters and following change of plaster, then the "dead space" exerts no pressure on the skin as does all the remaining plaster, and there is therefore, in most cases, blistering of the skin throughout the whole length of the tunnel. If the blisters rupture at the distal (toe) end of the cast, sepsis can extend throughout the whole length of the cast, as, for example, to the upper third of the thigh in a three-quarter plaster of Paris cast. I have seen a cellulitis of this whole area occur.

I may add that, having also visited many fracture centres in Great Britain recently, I found this method of removing plaster of Paris casts has been discarded for the reasons mentioned above.

Yours, etc.,

JOHN DICK.

Bellevue Hill,
Sydney,
February 27, 1943.

TRANSFUSION BOTTLES.

SIR: In THE MEDICAL JOURNAL OF AUSTRALIA of February 20, 1943, John A. McLean has reported an occurrence of accidental blockage of the air-outlet needle in the process of perforation of the rubber cover of a "Soluvac" bottle. Fortunately, in this case, an observant operator prevented any serious results, but such a satisfactory ending is unlikely to always follow.

In THE MEDICAL JOURNAL OF AUSTRALIA of April 19, 1941, the bottle for transfusion was described by me, which was claimed to be simpler in construction and use than any other existing type. No perforation of a rubber cover with needles is required in using this apparatus, and therefore the risk of a blockage such as that described by McLean is eliminated.

Yours, etc.,

D. L. BARLOW.

North Terrace and King William Street,
Adelaide,
March 2, 1943.

AN EASY WAY OF ISOLATING A HERNIAL SAC AND THE USE OF COTTON AND LINEN SUTURES.

SIR: Though I have never heard or read of a description of the method I use for finding, isolating and removing a hernial sac, it is so obvious and simple that it may be used by many and, for all I know (seeing but little surgical literature), may have been described often.

However, for the sake of those who sometimes find it hard to identify the sac as I used so often do myself, let me in all humility tell of something as elementary as Columbus's egg:

1. Perform the first two steps of Ferguson's operation for inguinal hernia as set out on page 608 of Binnie's "Operative Surgery" (eighth edition revised). On no account do the third step.
2. Retract the skin at the upper end of the wound and expose the peritoneum by splitting the aponeuroses for another inch or two.
3. Open the peritoneum and pack off the bowel should it be necessary.
4. Look for the mouth of the sac which will at once present itself.
5. Push a finger into the sac and, if it can be removed without dissection, remove it, but leave enough to reinforce the mouth when the latter is closed. Otherwise, split the sac and trim off as much of the wall as can be done without interfering with the cord and its vessels which are not disturbed throughout the operation and can, thus, never be injured by it.
6. Obliterate the mouth of the sac by sewing it up with linen thread or coarse cotton and include some of the flap in the suture to form a pad or plug.
7. Carry out the fourth step of Ferguson's operation to close the wound, using the same linen thread or coarse cotton to unite the aponeurotic layers with interrupted sutures and number 30 or 40 cotton to tie the vessels. The linen thread I am using is number 25 Glover's 3 cord thread.

Four years ago I saw Mr. Leo Doyle, of Melbourne, use silk sutures when doing an appendicectomy, and since then I have discarded catgut altogether except for perineal repairs and circumcisions where it obviates the removal of the sutures and disposes of my stock which will never be renewed. Instead, I used silk twist as long as I could easily get it; but, since the local stores have no more white silk, I use linen thread and fine cotton, the latter for sewing bowel and tying vessels and the thread for closing all layers of a wound except the skin, which is done with some kind of synthetic horse hair, though, when the latter is finished, I will use thread for the skin also.

I do not intend to revert to silk even when it is procurable, as, unlike linen or cotton, it loses its strength on boiling.

Until now, I have always used white or unbleached material, as I have been afraid that the colouring matter might be irritating to the tissues, and I do not use continuous sutures except sewing the bowel or the skin.

However, I have to admit that ends of the finer sutures are sometimes hard to see and pick up when they get blood-stained, and so it was most gratifying to read the article on "Cotton Suture Material" in your issue of February 27 and to learn it is safe to use black thread and cotton.

Since giving up the use of catgut, I have been astounded to find how rarely wounds (even those grossly contaminated with pus or bowel contents) have broken down; but the liberal use of sulphanilamide powder may have also been a big factor in this happy result.

Yours, etc.,

EDWARD HANLY,
Medical Superintendent and
Government Medical Officer.

Zeehan Hospital, Tasmania,
March 7, 1943.

A MEDICAL CRISIS.

SIR: The Victorian Bush Nursing Association has had and is experiencing much trouble from awards of different character, made by boards composed of city people who do not understand country conditions. The report of the National Health and Medical Research Council is an example of this character. In this case failure to understand not only country conditions, but also human nature. Every country dweller in Victoria knows that he cannot get a medical practitioner unless there is a hospital, and no medical man properly trained would try and develop a practice without hospital and nursing service.

The country man prefers Bush Nursing Hospitals because they are close to his home and provide doctor and excellent nurses and superb accommodation at a rate within his means. As private hospitals keep closing for various reasons, they are being replaced by Bush Nursing Hospitals at the request of the residents and doctors. It appears that shortly there will be only two kinds of hospitals in the country, the public hospital subsidized by the Government, and the Bush Nursing Hospitals which pay their own way, and, subject to the rules of the Association, manage their own affairs.

When the Department of Information found that the Bush Nursing Association had the lowest maternal mortality rate on the globe, one can understand the popularity of these hospitals. The Victorian Branch of the British Medical Association has issued a criticism of the report of the Medical Research Council, severe, I think, but more than justified. Let me give you an instance. In the Medical Research Council report, Benalla, Euroa *et cetera* are given prominence, but apparently they were not regarded as first-class country districts, and Edenhope was regarded as still lower. To anyone who knows Benalla or Euroa such an attitude is unbelievable.

Edenhope has an excellent Bush Nursing Hospital of medium size and asks for extensions, but Edenhope is sixty miles from any other hospital east or west; if they lost it, what would happen to the residents and their families? I can only express amazement at the report issued by the Medical Research Council, and I am sure that any attempt to implement it would raise intense feeling in the country. Have the members of the National Health and Medical Research Council ever seen a Bush Nursing Hospital? If not, I can provide facilities for such visits, and they can hear what country committees have to say about this proposal.

The select committee which has been taking evidence was asked by me whether any of them had seen a modern Bush Nursing Hospital. One member had seen one in New South Wales, where until recently they had been allowed (note the word) to have only two beds. At my invitation they visited the fine hospital at Ferntree Gully and met the three medical

practitioners and some members of the local committee. They expressed surprise at the existence of such a fine hospital, and at my suggestion made every inquiry, and finally sent me a most flattering report of the work of that institution. I deliberately stayed away so that they could satisfy themselves.

There are now 66 hospitals and 16 nursing centres, and applications for more hospitals are being received, and will be complied with when the nurses are available, and I may add when domestic help can also be obtained—though that to some extent is met by local voluntary help.

It only remains to point out that the personnel of the National Health and Medical Research Council consists of medical officers of health and laymen and that the medical man practising refused to sign the report.

The practice of medicine is facing a critical situation—it means government control as against freedom and independence.

Yours, etc.,

JAMES W. BARRETT,
Honorary Secretary, Victorian Bush Nursing Association.

Melbourne,
March 6, 1943.

Obituary.

JAMES ADAM DICK.

THE late Dr. James Adam Dick, whose death was announced in this journal some weeks ago, was known and respected by the medical profession throughout the length and breadth of Australia. He showed in his everyday life those qualities of heart and hand which are credited to the true follower of Æsculapius, and he was prepared to spend much of his life and energy in maintaining at a high standard the corporate life of the profession which he adorned.

James Adam Dick was born at Windsor, New South Wales. He became an undergraduate in the Faculty of Arts at the University of Sydney and graduated as Bachelor in 1886. He went to Edinburgh to study medicine and graduated as Bachelor of Medicine and Master of Surgery of the University of Edinburgh in 1890. He obtained his Licentiate in Midwifery at Rotunda in 1891 and his Doctorate of Medicine at Edinburgh in 1892. In 1901 he acquired the Fellowship of the Royal College of Surgeons of Edinburgh.

In 1893 Dick returned to Australia and started private practice at Randwick, New South Wales; he remained there till the day of his death. He had an enormous reputation in Randwick and neighbouring suburbs and his practice was commensurate with it. Moreover, he gained the confidence of his patients and kept it. In 1894 he became associated as honorary medical officer with the Home for Aged and Infirm, Randwick, and the Asylum for Children. He joined the British Medical Association in 1892 and in 1893 was transferred to the New South Wales Branch. At once he took a lively interest in its affairs and was elected a member of the Council in 1902; he remained on the Council as an ordinary member until 1936, when the Branch paid him the signal honour of appointing him Vice-President. In 1910-1911 he filled the office of President. He became a member of the Federal Committee of the British Medical Association in Australia in 1921, and in 1932 was its acting chairman. He was a member of the Federal Council from its inception in 1932 until 1936; during 1933-1935 he acted as Honorary Treasurer to the Federal Council. Dick was interested in medical congresses. He began in 1892, by reading a paper at the Intercolonial Medical Congress on obstetrical palpation, and at the Intercolonial Medical Congress of 1899 he was joint author of an article on bubonic plague. He was a member of the Executive Committee of the Australasian Medical Congress held in Sydney in 1911. He attended the Australasian Medical Congress at Auckland in 1914 and the Australasian Medical Congress at Brisbane in 1920. When the Australasian medical congresses came under the control of the British Medical Association, Dick was a vice-president of the Section of Naval and Military Medicine and Surgery of the first session in Melbourne in 1923. He was a member of the second session held at Dunedin, New Zealand, in 1927, a member of the third session held at Sydney in 1929 and a vice-president of the fourth session held at Hobart in 1934. He was a member of the fifth session at Adelaide in 1937.

From 1912 to 1932 James Adam Dick was a member of the Medical Board of New South Wales, which, though it served the community faithfully for many years, was treated far from well by the government of the day. He was a member of the Royal Society of New South Wales, and from 1898 to 1901 was joint honorary secretary of the medical section of that body. He was a councillor of Saint Andrew's College within the University of Sydney from



1925 to 1937. He saw active service in two wars—at the South African War from 1899 to 1902, and during the Great War from 1914 to 1919. Here he was mentioned in dispatches and was made a Companion of the Most Distinguished Order of Saint Michael and Saint George. In 1920 he received the Colonial Auxiliary Forces Officers' Decoration. As the commanding officer of a base hospital during the war of 1914-1918 he enjoyed the confidence and respect of many medical officers who were privileged to serve under him. Clearly James Adam Dick earned the admiration and esteem of his colleagues; the profession will remember him with gratitude.

HUGH CURRELL.

WE regret to announce the death of Dr. Hugh Currell, which occurred on March 11, 1943, at Mount Macedon, Victoria.

WILLIAM EDMOND RYAN.

WE regret to announce the death of Dr. William Edmond Ryan, of Rose Bay, which occurred on March 21, 1943, at Katoomba, New South Wales.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 50, of March 4, 1943.

ROYAL AUSTRALIAN AIR FORCE.

Citizen Air Force: Medical Branch.

Temporary Squadron Leader G. M. Oxer (1201) is granted the acting rank of Wing Commander whilst occupying a Wing Commander post, with effect from 1st January, 1943.

The following Flight Lieutenants are granted the acting rank of Squadron Leader whilst occupying Squadron Leader posts, with effect from 1st January, 1943: A. L. Kennett (1528), J. M. Alexander (1669), A. R. McCay (4371), R. M. Cloutier (4595), B. T. Mayes (4848).

Flight Lieutenant J. F. Hughes (2290) relinquishes the acting rank of Squadron Leader on ceasing to occupy a Squadron Leader post with effect from 1st February, 1943.—(Ex. Min. No. 61—Approved 2nd March, 1943.)

Australian Medical Board Proceedings.

QUEENSLAND.

THE undermentioned have been registered, pursuant to the provisions of *The Medical Acts*, 1939-1940, of Queensland, as specialists in surgery:

Kelly, Ronald William Grant, 447, Chapel Road, Bankstown, New South Wales.
Thompson, John Cyril, Kingaroy.
Millar, David Fitzroy, on active service.
Mason, Alfred Eric, on active service.

The undermentioned has been registered, pursuant to the provisions of *The Medical Acts*, 1939-1940, of Queensland, as specialist in pædiatrics:

Birchley, Herbert James, Ballow Chambers, Wickham Terrace, Brisbane.

The undermentioned has been registered, pursuant to the provisions of *The Medical Acts*, 1939-1940, of Queensland, as specialist in psychiatry:

Youngman, Norman Vincent, Dean Street, Toowong.

The undermentioned has been registered, pursuant to the provisions of *The Medical Acts*, 1939-1940, of Queensland, as specialist in gynæcology:

Millar, David Fitzroy, on active service.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Lawrence, Lorraine Cecile, M.B., B.S., 1942 (Univ. Sydney), 11, Milray Avenue, Wollstonecraft.
Royle, Norman James, M.B., B.S., 1940 (Univ. Sydney), "Moola", Pittwater Road, Pymble.
Mulvey, Margaret, M.B., B.S., 1940 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Gerrard, Gwendoline, M.B., B.S., 1936 (Univ. Sydney), 114, Ramsay Road, Haberfield.

Medical Appointments.

Dr. Robert Welsh Gibson, pursuant to the provisions of the *Health Act*, 1935-1941, of South Australia, has been appointed an Officer of Health at and around Tarcoola, South Australia.

Dr. Eric Hamilton White has been appointed deputy quarantine officer at Newcastle, New South Wales, under the provisions of the *Quarantine Act*, 1908-1924.

Books Received.

"Surgical Care: A Handbook of Pre- and Post-Operative Treatment", by R. W. Raven, F.R.C.S.; 1942. London: Edward Arnold and Company. 7½" × 5", pp. 279, with illustrations. Price: 10s. 6d. net.

"Vitamins in Medical Practice: A Survey of Present-Day Knowledge", issued by Roche Products Limited; Second Edition, Revised and Enlarged; 1942. Welwyn: The Broadwater Press Limited. 7½" × 4¾", pp. 30, with illustrations. Price: In Great Britain, 9d.

"The 1942 Year Book of Industrial and Orthopedic Surgery", edited by Charles F. Painter, M.D.; 1942. Chicago: The Year Book Publishers Incorporated. 7½" × 5", pp. 424, with many illustrations. Price: $3.00, post paid.

"The Vitamins in Medicine", by Franklin Bicknell, D.M., M.R.C.P., and Frederick Prescott, M.Sc., Ph.D., A.I.C., M.R.C.S.; 1942. London: William Heinemann Medical Books Limited. 9½" × 6¼", pp. 669, with many illustrations. Price: 45s. net.

"Textbook of Surgical Treatment Including Operative Surgery", edited by C. F. W. Illingworth, M.D., Ch.M., F.R.C.S.E.; 1943. Edinburgh: E. and S. Livingstone. 10" × 6¼", pp. 540, with many illustrations. Price: 28s. net.

Diary for the Month.

MAR. 30.—New South Wales Branch, B.M.A.: Council.
APR. 1.—South Australian Branch, B.M.A.: Council.
APR. 2.—Queensland Branch, B.M.A.: Branch.
APR. 6.—New South Wales Branch, B.M.A.: Organization and Science Committee.
APR. 6.—Tasmanian Branch, B.M.A.: Branch.
APR. 7.—Western Australian Branch, B.M.A.: Council.
APR. 9.—Queensland Branch, B.M.A.: Council.
APR. 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
APR. 20.—New South Wales Branch, B.M.A.: Ethics Committee.
APR. 21.—Western Australian Branch, B.M.A.: Branch.
APR. 22.—New South Wales Branch, B.M.A.: Clinical Meeting.
APR. 27.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

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